

Homilies for the Club of Rome

EARLIER this year, the organization which calls itself the Club of Rome achieved a notable publishing success with its document called *The Limits to Growth*, a popular account of the work done by Professor Dennis L. Meadows and his colleagues at the Massachusetts Institute of Technology on the application of Professor Jay L. Forrester's technique of model simulation to the analysis of the current social and economic trends in the world at large. Nobody will begrudge the authors of this book and their sponsors the sale of a few hundred thousand paperbacks, but from the start there have been serious doubts about the usefulness of computer simulation, at least as practised at MIT, in understanding the real world (see *Nature*, 236, 47; 1972). The Club of Rome and those who have confused its publication with the Mosaic tablets should therefore be given pause by the stream of technical comment on the document which has now begun. The article by Oerlemans, Tellings and De Vries on page 251 is the kind of criticism they will have to live with in the months ahead.

To be fair, it must be acknowledged that there is nothing inherently wrong in computer simulation, already an invaluable technique in several fields of management, and Professor Meadows is probably right to claim that his own model is among the most complicated so far developed. There are, however, serious questions as to whether even the MIT model can be complicated enough to simulate the real world in a way that is not misleading. There are also serious doubts about the validity of the assumptions made by the team at MIT both in setting up relationships between their mathematical variables and in the choice of initial conditions. Everybody knows that the output of a computer model is no better than the input. "Garbage in—garbage out" is the familiar slogan. What Oerlemans, Tellings and De Vries have done is to start with assumptions different from those of Professor Meadows and his team and to finish with different results. In itself, this is no surprise. But the results are also a good deal more cheerful than the apocalyptic projections of *The Limits to Growth*. And although there is no more reason to ascribe absolute validity to them than to those of the MIT studies, the fact that they differ so markedly from those of *The Limits to Growth* should be a powerful challenge to Professor Meadows and the Club of Rome. The pretence of objectivity surrounding the MIT study notwithstanding, it is now a proper question to ask whether the assumptions on which the MIT study was based were chosen, consciously or unconsciously, precisely so as to yield the gloomy projections which have chimed in so well with the present public willingness to believe that catastrophe is around the corner.

Informed criticism of the Meadows model is hampered by the continued absence of a full technical description of its assumptions. Although the team at MIT has provided laboratories elsewhere with copies of its computer programs, the assumptions remain *ex cathedra* and

unjustified. Earlier this year, Professor Meadows was promising that a detailed technical report would be available in the autumn. If he and his colleagues are to hold up their heads in professional circles, it is to be hoped that their fuller document will appear soon. But even on the basis of the scanty information provided in *The Limits to Growth*, it is clear that the model at MIT has several structural weaknesses, of which Oerlemans, Tellings and De Vries provide a useful classification.

They make a particularly telling point when they complain, as an illustration of the model's lack of empirical content, that it is hard for ordinary mortals to understand how a single variable can represent worldwide pollution. "Who can say what the height of the 1970 global pollution level . . . should be in relation to the 1900 level?" In the Meadows model, the pollution variable is a function of total population and industrial output *per capita* but, so far as can be told, no allowance has been made for the moderating influences of the public policies already well in train that are certain to soften whatever relationship there may be between the intensity of industrial activity and the pollution of the environment. Yet in the calculation of catastrophe and collapse which is a central theme of *The Limits to Growth*, global pollution, defined somehow as a number, plays a crucial part. For it has been assumed that above a somewhat arbitrarily chosen worldwide pollution level, there will be a negative correlation between pollution and life expectancy. In other words, as soon as industrial output *per capita* exceeds a certain value, people will start dying off from the consequences of the pollution. No wonder the MIT model leads to catastrophe and the collapse of the population of the world. Oerlemans, Tellings and De Vries are right to argue that in an attempt to construct a computer model of the world, great care should be taken to describe the world in terms of arbitrary constructs such as global pollution level. Using the language of Meadows and his mentor Forrester, but making assumptions about the extent to which capital resources will in future years be devoted to the abatement of pollution, Oerlemans, Tellings and De Vries are able to show quite simply that the pollution feedback loop in the Club of Rome's computer model is much less vicious in its effects than Meadows *et al.* pretend.

Another serious weakness of *The Limits to Growth* is the set of assumptions made about natural resources. To be sure, on the face of things, Meadows and his colleagues have been more prudent than other prophets of calamity. They have, for example, assumed in what they call their "standard run" that there are resources enough to last for 250 years at the rate of consumption in 1970. Because the known reserves of some materials such as copper and lead are enough to last for only 36 and 26 years respectively at the 1970 rate of consumption, this assumption appears to be generous. Yet in its handling of natural resources, the MIT model is dangerously over-



simple. For one thing, it includes no allowance for the way in which increasing scarcity will provide incentives for further exploration, discovery and the more economical use of natural resources. Worse still, the model lumps together all natural resources in a single computer variable, thus denying not merely the possibility but the historical experience of the progressive substitution of one material by another. Oerlemans, Tellings and De Vries point to another weakness in this conceptual structure—"One may wonder whether uranium was a resource in 1900 and what things not at present thought of as resources will become resources before the year 2100" (by which time the Meadows projections imply collapse). They find it comparatively easy to modify the computer models so as to show that the exhaustion of natural resources need not be nearly as abrupt as Professor Meadows and his colleagues suggest.

Few people will be surprised that these modifications have been possible, but this work, like that of other groups now investigating computer stimulation of the world, does raise serious questions about the role of exercises like these in the forecasting of the future. The first question to ask is whether the output of the computer models should be regarded seriously as forecasts of any kind. Professor Meadows and his colleagues have repeatedly insisted that their work is not a means of predicting the future but, rather, as a projection into the future that will be realized only "if present trends continue", the conventional disclaimer of the doomsday men. But Meadows and his colleagues have been exceedingly selective in their choice of present trends. They cheerfully incorporate in their model the present trend of worldwide population growth but make no allowance for the possibility that the demographic transition which has changed the demographic pattern of western Europe in the past century will occur elsewhere. They ignore the equally recognizable "present trends" which consist of continually increasing expenditure on the abatement of pollution and the steady transformation of the pattern of use of natural resources embodied in substitution, recycling and exploration. They leave out of their computer calculations the consequences of technological change which, for the best part of two centuries, have made it possible to blunt the edges of the problems with which they are preoccupied.

But is not the MIT model better than any other computer model? And is not a computer model, almost by definition, better than the kinds of models which people construct in their heads and which often masquerade under the label of political decision? This is the defence on which Professor Meadows has often, in the past few months, relied. On the technical level, he is right, for his model is splendidly intricate. But it is also clear that the problem of describing the real world is much more difficult than he allows. Not merely is it foolish to attempt to represent the effects of pollution on the human life span by a single number but, on the strictly technical level, there are limits to what can be done to relate age-specific death rate to nutrition. And when it comes to making assumptions about the way in which people will in future choose to devote capital resources to industrial investment, agricultural investment and personal consumption, Professor Meadows and his colleagues are seen to have begged more questions than they have formulated, let alone answered. In this sense, Oerlemans, Tellings and De Vries are right when they say that if

computer modelling of the world as a whole is to be successful, there will first have to be much more thorough investigation of the social, economic and technical basis of the assumptions on which such models are necessarily based. Delicately, they refrain from pointing out that this programme of investigation is no less than the whole of what the social scientists have recently set their sights on. Until that work is further advanced, the work of Professor Meadows and those who would imitate him is bound to run the risk of deserving Professor Gunnar Myrdal's epithet, "pretentious nonsense". In passing, it should be observed that the reputation of computer simulation and even of objective investigation as such—which means the whole of science—is likely to be damaged if computer models go about the world pretending that their investigations have a validity which, in truth, they lack.

All this amounts to or should amount to a serious challenge to the Club of Rome. In the excitement over the publication of their first paperback, the members of the club's executive committee put out a string of policy recommendations, sometimes naive, sometimes platitudinous but sometimes sensible, which were meant as a recipe for the avoidance of catastrophe. In retrospect as at the time, it is clear that the Club of Rome was using the occasion of Professor Meadows's computer simulation as a peg on which to hang a number of well-intentioned declarations as to the directions in which the world should change. The executive committee, for example, was anxious to see more foreign aid for developing nations, a position to which less exalted people have stumbled without the help of a computer model. Similarly, it is fierce on the need somehow to contain the growth of the world's population, an urgent need even without the help of apocalyptic projections by computer. So would it not now be seemly that the Club of Rome should say what it might have done in the first place—that it has a clear view of the directions in which it would like to see society progress, to acknowledge that some (but not all) of these are contentious and to confess that the computer modelling which it has been sponsoring, apparently at some expense, is for the time being at least so irrelevant that it is neither here nor there.

100 Years Ago



Bree on Darwinism

PERMIT me to state—though the statement is almost superfluous—that Mr. Wallace, in his review of Dr. Bree's work, gives with perfect correctness what I intended to express, and what I believe was expressed clearly, with respect to the probable position of man in the early part of his pedigree. As I have not seen Dr. Bree's recent work, and as his letter is unintelligible to me, I cannot even conjecture how he has so completely mistaken my meaning: but, perhaps, no one who has read Mr. Wallace's article, or who has read a work formerly published by Dr. Bree on the same subject as his recent one, will be surprised at any amount of misunderstanding on his part.

August 3

CHARLES DARWIN

From Nature, 6, 279, August 8, 1872.

OLD WORLD

Nuclear Industry and the Select Committee

THE British Government is to make a statement on the reorganization of the nuclear power industry, and on the type of reactor Britain is to build next, before Parliament rises on August 9 (crises permitting). Mr Tom Boardman, Minister for Industry at the Department of Trade and Industry, said as much before the Select Committee on Science and Technology last week. But he would not promise firm decisions. "I hope to be able to present matters more clearly" was all he would say.

Nevertheless, there is a prospect that the nuclear power industry is due for a radical reorganization. At present it consists of two consortia, British Nuclear Design and Construction Ltd. and The Nuclear Power Group Ltd, with British Nuclear Fuels providing the fuel. "Few would defend the consortia", Mr Boardman said, "and there is general agreement that there should be a change". Merging of the two consortia seems the likeliest course, particularly as Mr Boardman added that "there are not likely to be enough home orders [for nuclear power stations] to keep competition between the two going". The Central Electricity Generating Board agrees to the proposed merger, Mr Boardman indicated, although in evidence to the select committee in 1966 and 1967 the CEBG had insisted that competition in the supply of reactors was vital.

But if Mr Boardman conceded that the consortia are likely to be merged, he would not say how this is to be done. Without actually denying rumours that Sir Arnold Weinstock of The General Electric Co. Ltd., the dominant shareholder in the larger of the two consortia, is to reorganize the nuclear industry, Mr Boardman stated categorically that the rumours did not stem from his department, and that neither Sir Arnold nor anybody else has as yet a remit from the government. Patently, the select committee hoped that whoever got the job it would not be Sir Arnold—he would, the committee felt, be a "mistake".

The committee also held that buying reactors from the United States—a policy that the committee fears Sir Arnold would follow—would be "disastrous". Did Mr Boardman agree? Mr Boardman did, but it soon became plain that he would only regard it as disastrous if American light water reactors were bought to the ex-

clusion of all other types; Britain could still develop the High Temperature Reactor (HTR) and fast breeder, he said, hastily pointing out that this is simply one of the alternatives before the government and not necessarily the one that will be chosen.

Mr Peter Vinter, chairman of the Department of Trade and Industry's thermal reactor review committee, who

appeared with Mr Boardman before the select committee agreed that "disastrous" would not be the right word for buying American so long as Britain continues to develop its own reactors. Buying PWRs (pressurized water reactors), Mr Vinter said, would open up export markets which are not available to Britain at present, although he added a caveat that fuel for ex-

SOVIET SCIENCE

Soft Landing

from our Soviet Correspondent

THE Soviet probe, Venus-8, soft-landed on the illuminated side of Venus on Saturday, July 22. This probe, of identical mass (1,180 kg) and, apparently, of identical external design to the previous probe, Venus-7 (see figure), which made the first soft landing on the planet on December 15, 1970, seems to have an improved transmitting apparatus which enabled the probe to transmit for 50 min compared to 23 min for the first probe. The experiments on Venus-8, however, differed in intent from those of its predecessor which, unlike Venus-8, landed on the dark side of the planet.

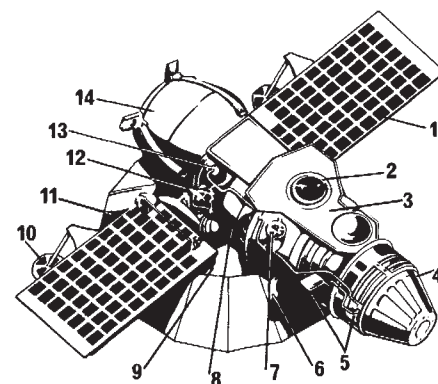
Dr M. Ya. Marov, director of the Venus-8 scientific programme, interviewed in *Pravda* (July 23, 1972), said that the principal interest is the difference in physical conditions on the day and night sides of the planet. From radio astronomical observations, he said, an atmospheric temperature difference of only about 1° C is thought to exist; if the Venus-8 observations confirm this difference (which is negligible for surface temperatures of the order of 500° C), such a result would be highly significant for any theoretical model of the Venusian atmosphere, because it would imply both a very high specific heat and intensive processes of gas-mixing. Large differences may possibly occur, however, at high altitudes and it is therefore important to obtain a temperature and pressure profile for the atmosphere.

Another entirely new project is an experiment designed to determine how much sunlight reaches the surface of the planet. These results are expected to raise further questions on the mechanism of the penetration of sunlight through the cloud-cover, the effect of this penetration on the temperature gradient of the atmosphere, and if sunlight does

penetrate to the surface, the possible effects of "superdiffraction" produced by the enormous atmospheric pressures at the surface.

Another experiment described by Dr Marov is one to measure trace gases (nitrogen, water-vapour and oxygen) in the 97% CO₂ Venusian atmosphere. Although the four preceding Venus probes provided data for these gases, it would seem that Soviet planetologists are not entirely satisfied with the results, and require further confirmation, particularly for the lower levels of the atmosphere which are not amenable to spectroscopic study from Earth.

So far, official releases state little more than that during descent and after landing the experiments worked satisfactorily, and that detailed data will be published in due course. They do, however, mention one detail not indicated by Dr Marov—that in addition to its atmospheric observations, Venus-8 also transmitted information on the nature of the Venusian surface.



Soviet Venus-7 probe: 1, Solar panel; 2, Stellar orientation sensor; 3, Protective panel; 4, Correcting motor unit; 5, Pressure system nozzles; 6, Cosmic particle counter; 7, Solar orientation sensor; 8, Orbital section; 9, Radiator cooler; 10, Wide beam antenna; 11, Narrow beam antenna; 12, Pressure control unit; 13, Compressed nitrogen tank; 14, Descent stage.

ported British PWRs would be supplied by the American designers, "and that is worth a lot of money".

Asked why his report could not be published, Mr Vinter replied that it contained much confidential information. People in the industry would not have talked freely if they thought their opinions would be published; the DTI would have to continue to work with the industry after future policy was decided, and so must not betray the industry's trust.

Questioned about the conclusions of his eighteen-month study of alternative reactor types, Mr Vinter had nothing to say. Part of the trouble is that no one system comes out clearly on top when all the criteria are applied. These are cost, performance (both known and expected), safety, environmental impact, possibilities for international collaboration, time involved in finishing experimental designs and last, but not least, the requirements of the electricity generating boards. Mr Vinter added that it became apparent in the later stages of this study that the choice of reactor could not be separated from the organization of the industry and so his committee, although it had been set up simply to determine the most suitable reactor type for Britain, also examined the structure of the industry.

But in spite of frenzied speculation, Vinter's conclusions and Boardman's decision remain well shrouded secrets until the minister makes his statement. All the select committee extracted from him was a promise that when the statement is made the "basis for the decision will be revealed".

AGRICULTURAL INSTITUTES

Animals and Plants

LIKE a voice from a past world, the biennial report of the Agricultural Research Council's Institute of Animal Physiology at Babraham outlines the institute's work untroubled by the shadow of Rothschild and the government's scythe—the ARC is the council hardest hit by the government's white paper on research and development.

The ARC observes that the institute's work is "generally of greater scientific than agricultural interest in its early stages and to single out the institute's strictly practical achievements gives a somewhat misleading picture of its activities", but otherwise there is no hint that Rothschild has spoken. What the report does give is a detailed analysis of the institute's work with a chapter reviewing work on animal behaviour. Dr B. A. Baldwin declares that animal behaviour is a relatively new field of scientific study, embracing zoology, psychology and physiology, which can offer consider-

able economic benefits. Much more is known about the behaviour of rats than of farm animals, he says, an imbalance that the institute is trying to correct. Among the current work at Babraham is a study of thermoregulation in pigs and maternal behaviour in sheep, the latter showing that ewes and lambs can recognize each other's calls. Working with male rats and cats the institute has found that the compound parachlorophenylalanine (PCPA) temporarily blocks the formation of 5-hydroxytryptamine, resulting in increased sexual activity, and that behavioural studies of animals subjected to intensive husbandry should provide a better basis for evaluating such husbandry.

The fundamental research at the institute includes studies of sodium

channels in nerve membranes and of the ultrastructure of immunoglobulins. During the two year period covered by the report, the institute's staff produced more than 260 papers and almost 100 other publications, and the new Greville Laboratory for biochemistry was opened.

Rothamsted Experimental Station has also produced its annual report, a two-volume production listing the work of the station's thirteen departments and two farms, and of the Broom Barn experimental station. The report shows that the Soil Survey of England and Wales is proceeding steadily, with thirty-eight areas under study during 1971. Twelve maps at 1:25,000 have now been published with accompanying Soil Survey records for nine of them.

Spassky Falling Below Form

THE seventh game of the Spassky-Fischer match was a rather wild but very entertaining battle. Spassky allowed Fischer to play one of his favourite variations with black in the Sicilian Defence, a line that involves the capture of a pawn at the expense of a slight loosening of his king's position, and made several bold thrusts in the early stages of the game. Fischer defended coolly, however, reorganizing his pieces and forcing the exchange of queens while still hanging on to his extra pawn. This is the situation in the diagram after Black's 27th move. Fischer seems poised to secure a complete consolidation of his position, and one would normally have expected him to win by virtue of the extra pawn.

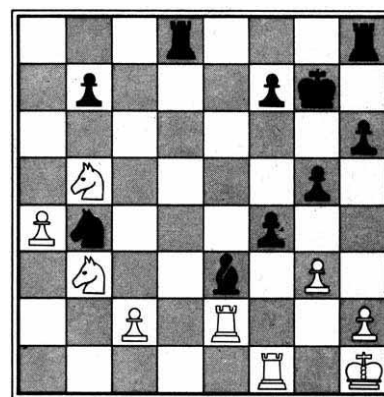
At this point, however, Spassky conceives a plan of desperate ingenuity based on an obscure knight manoeuvre that aims to throw the position into confusion once again. The plan succeeds admirably, and Fischer makes a few rare inaccuracies to allow Spassky to reach a position by the 40th move (the end of the first session) where he must even have had some hopes of victory. Adjournment analysis, however, apparently convinced both players that a draw was the natural outcome.

The eighth game was a disappointing anti-climax to the previous one. Spassky played well below his normal form and committed two serious blunders in fairly quick succession as early as the 15th and 19th moves. The outcome of these errors was that Fischer was presented with the advantage of the "exchange" and he was able to convert this into a win by accurate technique.

The match has already reached a critical stage for Spassky since he is now trailing by a two point margin (5 points to 3), and his play has shown distinct signs of fatigue and demoraliza-

tion. Spassky was obviously well advised to take one of his three available options (technically on medical grounds) of postponing a game, in the hope that he can return refreshed to the battlefield. J.P.

FISCHER BLACK



WHITE SPASSKY

SEVENTH GAME White: Spassky Black: Fischer Sicilian Defence

White	Black	White	Black
1 P-K4	P-QB4	26 QxQch	NxQ
2 N-KB3	P-Q3	27 R-K2	K-N2
3 P-Q4	PxP	28 R-N5	P-N3
4 NxP	N-KB3	29 N-B4	N-Q4
5 N-QB3	P-QR3	30 N(B4)-Q6	B-B4
6 B-KN5	P-K3	31 N-N7	R-QB1
7 P-B4	Q-N3	32 P-B4	N-K6
8 Q-Q2	QxP	33 R-B3	NxP
9 N-N3	Q-R6	34 PxP	P-N5
10 B-Q3	B-K2	35 R-Q3	P-R4
11 O-O	P-R3	36 P-R3	N-R4
12 B-R4	NxP	37 N(N7)-Q6	BxN
13 NxN	BxB	38 NxB	R-B8ch
14 P-B5	PxP	39 K-N2	N-B5
15 B-N5ch	PxB	40 N-K8ch	K-N3
16 NxPch	K-B1	41 P-R4	P-B3
17 NxB	N-B3	42 R-K6	R-B7ch
18 N-Q6	N-Q1	43 K-N1	K-B4
19 NxP(N5)	Q-K2	44 N-N7ch	KxP
20 Q-B4	P-KN3	45 R-Q4ch	K-N6
21 P-R4	B-N4	46 N-B5ch	K-B6
22 Q-R1	B-K6ch	47 R(6)-K4	R-B8ch
23 K-R1	P-B5	48 K-R2	R-B7ch
24 P-N3	P-N4	49 K-N1	
25 QR-K1	Q-N5		

Drawn by perpetual check

Work on synthetic pyrethroids (see *Nature*, **233**, 441; 1971) has continued, with the station attempting to discover their mode of action; first results suggest that the knockdown and lethal effects arise in progressive stages at one site in the central nervous system, rather than from two separate actions, one peripheral and one central. More detailed knowledge should help produce yet more active compounds. Studies of biochemical changes in maturing fruit, of algal nitrogen fixation, of the effect of temperature on grain growth in wheat, of potato cyst nematodes and of bees are just a few of the many projects detailed in the report. In the course of the year the staff published more than 300 scientific papers and the second part of the report contains eleven detailed papers on various aspects of the station's work, including the Rothamsted Insect Survey and the Agdell experiment which has run since 1848, to study the effects of crop rotation and the accumulation of phosphorus and potassium from fertilizers.

HIGHER EDUCATION

Architects in Trouble

THE Architectural Association's school is firmly in the doldrums again. Late last month, Mrs Margaret Thatcher announced, in reply to a question in the House of Commons, that local education authorities need no longer pay the school's tuition fees of £580. As a result, 125 students who have been awarded places for the coming academic year are left in limbo, not knowing if they will receive grants, and the school stands in danger of having an essential part of its colourful character destroyed.

The past history of the AA is nothing if not chequered. The school is independent—fiercely so—with a considerable reputation in architectural circles backed by a system of government that actually puts into action all the pious lip service normally paid to student participation. It is governed by a Forum elected by students, staff, the association's council and membership. Its troubles have stemmed from the British system of financing higher education by which maintenance grants and nominal tuition fees for each student are paid by local education authorities, while universities and colleges receive further direct grants from the government. As a result it costs an LEA between £90 and £180 a year in fees to send a student to a conventional university or college, but £580 to send a student to the AA which, because it receives no state subsidy, has to charge a realistic fee.

Not surprisingly, some LEAs object to

paying four to five times the norm just to send a student to the AA. The school points out however that the real cost of sending a student to university is about £900 by the time central government grants are taken into account, so that its fees of £580 are really rather cheap.

So far, the LEAs have paid the fees, even agreeing to an increase last year after attempts to merge the school with Imperial College fell through. But now it is revealed that the rise was only agreed on condition that within the year the school would reduce its fees to £180. For an institution like this, with no appreciable income other than its students' fees, this was clearly impossible.

Instead, the school promised the LEAs that it would not increase its fees for another five years. The LEAs still said they could not pay, so in May the school approached the Department of Education and Science, asking it to make up the £400 difference between the £180 the LEAs were willing to pay, and the £580 that the school needs.

The DES granted the school a brief audience in June and accepted a letter outlining plans for the next ten years and asking for the £400 grant—pointing out that over five years this would cost the DES about £80,000 a year and over ten years about £100,000 a year, allowing for a fixed number of grant-financed students.

The next the school heard about its proposals was when Mrs Thatcher informed it of the contents of the Commons statement the day before it was made. In her statement Mrs Thatcher refused the grant and freed the LEAs from their mandatory commitment to pay the school's fees, although she hoped that the authorities "will be generous in exercising their discretion in favour of students who were expecting to enter the school this year".

Damaging though the blow is, it does not sound the school's death-knell. By increasing the number of self-supported and overseas students the school can continue, although much of its character will change as it becomes a rich man's academy. There is also hope, however, that the LEAs may continue to pay the fees voluntarily. The Inner London Education Authority has already agreed to do so for the coming year, although this only affects a few of the 125 stranded students, and ten other students have already received grants. In an effort to rescue the remainder the school has written to the eighty local authorities to which this year's intake belong, asking them to finance the students at least for this year, giving the school another chance to prove its case in the coming academic year.

But unless Mrs Thatcher can be persuaded to revise her decision—and there are precedents for the sort of grant for which the AA is asking—or unless the bulk of the LEAs agree individually to continue to pay the fees, then the school may in time cease to be the vibrant force it is at present in the architectural world. But if the outlook for the school is somewhat bleak, the outlook for the 125 students who were hoping to enter the school this September is even grimmer if the LEAs refuse them grants. At this late stage it will be hard to find places at other architectural schools.

BIRTH CONTROL

Sydney Congress

IMPLANTING a fertilized human egg in a foreign uterus raises fewer ethical problems than adoption, according to Sir Alan Parkes, director of the Galton Foundation. Sir Alan was supporting Dr Malcolm Potts, medical director of the International Planned Parenthood Federation, in discouraging melodramatic interpretations of the work of Dr R. G. Edwards and colleagues at the University of Cambridge on *in vitro* fertilization of human ova. The implications of a childhood spent in another woman's house, said Sir Alan, are much more serious than those of a mere nine months in another woman's uterus.

Sir Alan was speaking in London at a meeting called to publicize a congress to be held in Sydney this month under the sponsorship of the Australian Family Planning Association and the South East Asian and Oceanic divisions of the IPPF. The topics to be discussed in Sydney include new intrauterine devices incorporating copper which have reduced side effects but have an increased failure rate, vasectomy, the experience gained in the United States with surgical out-patient abortion, and the Asian experience with prostaglandins.

Out-patient abortion, according to Dr Deys, is both simple and free of undue trauma for the patient. The patient must, however, first be properly screened but the operation only takes about five minutes. Out-patient abortion by the suction technique can, however, only be used up to the eleventh week of pregnancy. After this it is still an open question whether or not the new prostaglandins or surgery is to be preferred, according to Dr Potts. Prostaglandins applied directly to the uterus are satisfactory in general but sometimes fragments of the placenta are left behind and surgery becomes necessary, cancelling out the benefit of prostaglandin treatment.

NEW WORLD

Canada's Hard Look at Big Brother

by our Washington Correspondent

Ottawa, July

LAST year Dr Gerhard Herzberg was awarded the Nobel prize for chemistry, a distinction that has made him almost a household name in Canada and internationally one of the country's best known scientists. But the chief significance of the event is that Herzberg is the only Canadian working in Canada to receive a Nobel prize. Canada's success in the Nobel stakes has been a long time coming.

To many people in Canada, the novelty of such international recognition of the quality of Canadian science is an indication that the country's scientific resources are being inefficiently managed for it is a fact that Canada's contribution to the total amount of basic research in the world is not matched by a proportional share in the world's scientific awards. And, crude as this indication may be, it has been reinforced recently by a variety of reports and statements from a number of different committees, establishments and individuals who have been analysing Canada's science policies and industrial strategies.

To an observer, the issues being debated in Canada are common enough—the need to stimulate industrial innovation, the desirability of coordinating the activities of the universities, government and industry, the question of matching the output of graduates from the universities with the number of available jobs and the problem of deciding which scientific projects to back with a limited amount of money. But there are many aspects to the debate in Canada which are unique, and which are chiefly a product of its coexistence in the North American continent with the United States—a factor that inevitably affects almost every aspect of Canadian life.

One obvious result of the proximity to the United States is the high level of US investment in Canadian industry, and the large influence of subsidiaries of US based multinational corporations on the Canadian economy. These factors have shaped Canadian science policy in many ways, some of which are only now being recognized, and they also present monumental—some say insuperable—obstacles to attempts by the Canadian government to alter the country's industrial strategies.

As far as research and development are concerned, the presence of many foreign-owned firms on Canadian soil has both direct and indirect effects on

SCIENCE IN CANADA

Our Washington correspondent will have more to say about Canada next week.

the levels of expenditure on industrial science and technology. For one thing, in many multinational corporations, research and development tend to be performed in one place—usually the country in which the corporation has its headquarters—which tends to make the subsidiaries chiefly assembly plants and marketing organizations geared solely to one national market. In Canada, this has tended to depress the level of expenditure on research and development.

But it has also tended to fragment the Canadian market and, according to some observers, to make Canadian industry inward-looking and lacking in entrepreneurial spirit. The fragmentation is brought about chiefly because of the relatively small costs of setting up and operating subsidiaries of US based multinational corporations: physical proximity to the United States, the similarity of the markets and spillover of advertising reduce operating costs which in turn requires a smaller market to produce a profit. Consequently, foreign-owned subsidiaries are easier to set up and are often more viable in Canadian firms.

Another aspect of the proximity of US technology is that Canadian firms have often been able to buy technology under licence, which has provided little incentive for Canadian firms to undertake research and development themselves. As Mr. Alastair Gillespie, Minister of State for Science and Technology, puts it, "We have been able to enjoy the benefits of technology without having to do a lot ourselves—it's a lot simpler to enter a licensing agreement than to do the research ourselves". In short, many observers and critics of Canadian science policy during the past few years have suggested that Canada lacks its own technological base and provides a poor climate for innovation.

The upshot is that the pattern of expenditure on science and technology in Canada has a number of significant, even alarming, features. For example, the total expenditure of about \$800 million a year on science and technology in Canada is divided roughly in the proportions 23 per cent to basic research, 38 per cent to applied research and 39 per cent to development. In comparison with the United States and the United Kingdom, for example,

Canada's pattern of expenditure is weighted heavily in favour of basic research and is very low on development—the US expenditures are divided approximately into a 14 per cent for basic, 22 for applied and 64 for development, while the UK spends 11, 24 and 65 per cent on these activities respectively. Moreover, among the member countries of the Organization for Economic Cooperation and Development and development performed by government and lowest in the proportion performed by industry. The percentages are 35.6 and 37.7 per cent respectively, compared with 14.5 and 69.8 per cent in the US and 24.8 and 64.9 in the UK. Canada also ranks ninth among the 10 OECD countries in the proportion of its GNP which is devoted to research and development—about 1.4 per cent.

During the past few years, however, there has been a growing realization in Canada that the country's scientific and technological efforts may lack some direction and may be weighted too much towards basic science and government establishments, and there have been three developments which address these problems. The first was the setting up in 1966 of the Science Council of Canada, an advisory body reporting to begin with directly to the Prime Minister, composed of scientists and administrators from industry, government and academe and charged with the task of examining and advising on all aspects of Canadian science policy. At about the same time, a special committee of the Senate was also set up to inquire into Canada's science policy. The committee, chaired by Senator Maurice Lamontagne, a senator from Quebec, an economist and a member of the Club of Rome, has produced two very controversial reports and is working on a third. Finally, a year ago, a Ministry of Science and Technology was set up, partly as a result of recommendations from both the Science Council and the Lamontagne committee. The new ministry, headed by Mr Alastair Gillespie, is a small policy-making body which operates no laboratories of its own and gives no grants, but which exercises what can best be described as advisory oversight of the scientific and technological activities of the federal government. Gillespie has a seat in the cabinet and derives most of his formal power from his membership of the Treasury Board—the chief holder of the Federal government's pursestrings.

During its six-year lifetime, the Science Council has produced an avalanche of reports, statements and

recommendations, but it is difficult to ascertain just how effective it has been in increasing public awareness of science policy issues or in getting its recommendations accepted. The Lamontagne committee, on the other hand, has touched off a vocal reaction to its recommendations, and has taken the science policy debate into the newspapers and other public media. As one staff member of the Science Council admitted, "when I was in University, I used to see the Science Council reports gathering dust on the book shelves, then along came Lamontagne, he issues one report and everybody is talking about it." One of the sharpest criticisms of the Lamontagne committee's proposals has, in fact, come from the Science Council itself.

The Lamontagne Committee issued its first report, a critical review of the history of Canadian science policy, in December 1970, and followed it up with a second report in January this year, entitled *A Science Policy for Canada: Targets and Strategies for the Seventies* (see *Nature*, 235, 243; 1972). The first report painted a very bleak picture and suggested that Canada has no recognizable science policy, while the second argued the case for a coherent science policy and a set of specific objectives. Like the Rothschild Report in the UK, the second volume of the Lamontagne Report has been most unpalatable in the universities.

Essentially what the Lamontagne Committee suggests is a reorganization of the federal government's laboratories into a new administrative network, a gradual increase in expenditures on research and development until it reaches 2.5 per cent of GNP in 1980 and 3.0 per cent by 1985, and a shift in emphasis towards applied research, so that by 1980 only 10 per cent of the total national research and development effort will be devoted to basic research. As for industrial innovation, Lamontagne points out the lack of entrepreneurial spirit and the fragmentation of the market, and suggests that industry itself should set its house in order by setting up task forces to address questions of rationalization of industries and markets. Like Rothschild, he also suggests that the federal government should contract out much of its applied research to industry and universities.

On government-sponsored research and development, the Lamontagne committee made a series of novel recommendations, and these have drawn some of the sharpest fire. The suggestion is that three foundations should be set up to provide grants to universities and similar institutions for curiosity-oriented research, and that the foundations be drawn together under the umbrella of a Canadian Research Board. This proposal would split the granting

functions away from the National Research Council and integrate them with the Medical Research Council and the Canada Council. The committee also suggests that the basic research activities performed by agencies of the federal government be grouped together into a national research academy, which would perform much of its work at the request of government agencies and private firms on a fee paying basis. Finally, the industrial research activities of the federal government should be grouped together into yet another organization called the Canadian Industrial Laboratories Corporation, which would report to the Minister for Trade, Industry and Commerce.

In short, the committee draws a distinction between basic and applied research activities of the federal government and treats them separately, and also suggests that to provide closer links between government, the universities and industry as much work as possible should be contracted out.

The Science Council, however, takes issue with nearly all of this. First, the council questions the very basis of the committee's proposals by suggesting that the concept of a coherent science policy is unrealistic, because what Canada needs is a series of science policies which take into account the different priorities in different regions of the country. It also argues that no specific goal should be set for the level of expenditure on research and development. Rather, the council reiterated in a report made public last month, "the funds which are allocated to scientific activities annually should be granted, program by program, in face of competition from other potential users of these funds, with each program justifying its expenditure on economic, social or cultural grounds. The 'R&D budget' would then become the sum of the allocations of funds to individual programs and activities."

Having blasted one of the chief principles on which the Lamontagne Committee's recommendations are based, the Science Council then goes on to criticize the proposals for setting up a national research academy and an industrial laboratories corporation. For one thing, the Science Council dislikes the arbitrary distinction drawn between basic and applied research, and for another, it is opposed to stripping some research activities away from departments. What is needed to make departmental programmes more relevant to their missions, the Science Council suggests, is better management and direction in the departments themselves. The Science Council does, however, agree that the granting functions should be split off from the National Research Council, but is not happy about the suggestion

that the proposed foundations should restrict themselves to supporting only basic research, because this would "lead to endless and useless arguments on the classification of research as basic or applied, free or oriented."

Underpinning much of the Science Council's response to the Lamontagne Committee's report is the belief that the new Ministry of Science and Technology may provide much of the coordination and rationalization of government policies for science and technology. Gillespie, who is at the centre of the science policy debate, has however, declined to make many public comments on the Lamontagne report, and especially on its recommendations for the National Research Council and government research and development.

Gillespie said in an interview, however, that he accepts in principle the senator's suggestion that Canada may be performing too little applied research, and that he believes that the principle of contracting out government research to industries is a valid approach. To this end, the government will soon announce that all federal departments and agencies must in future consider whether or not new research and development projects can be contracted out. They will have to clear this in advance, and the Ministry of State for Science and Technology will play the chief role in the determination. The new plans, Gillespie suggested, "should provide a better relationship between government, industry and the universities, and it should put more government research in industry where its potential use can be determined". One problem, however, is that with the preponderance of US subsidiaries in the Canadian economy, the Ministry for Science and Technology must be careful about getting itself into the politically sensitive area of giving government grants to foreign companies.

But that is not the only politically sensitive area which the new ministry must beware of. The ministry is only one year old, and since it is charged with the task of ensuring that the federal governments fit in with national objectives and to help set priorities for scientific expenditure, it is likely to run up against departmental jealousies. Gillespie can, in the last resort, exercise his power on the treasury board to establish the ministry's policies, but he says that he prefers not to set himself up as an overlord. The ministry is intending to influence policy more behind the scenes by reports and advice. Its future and influence will clearly depend on the quality of the staff it attracts, and especially on the quality of its early advice. As one member of the Science Council remarked, "at this stage, the minister can make more enemies than friends."

NEWS AND VIEWS

Atomic Clocks Coming and Going

SOME time ago when Weber's experimental results on gravitational waves were first announced in the newspapers, I had a physicist from central Europe working in my department at Queen Elizabeth College, London. With some excitement I told him of Weber's detection of gravitational waves. He looked at me with surprise and said, "But we already *know* from general relativity that gravitational waves exist". It was, I suppose, the difference between an empiricist and a rationalist.

Hafele and Keating now report (*Science*, 177, 166; 1972) experiments on the transport of atomic clocks round the Earth in fast aircraft. They find that the time recorded on a clock which has been flown round the Earth differs from that on a clock which has remained Earth-bound in the meantime; and that the time on the flying clock depends on whether the circuit is easterly or westerly.

As an empiricist I am very glad to have these results, though I feel their chief value (with one qualification to be mentioned later) must be the propagandist one of helping to convert those who still believe there is a clock paradox. I think one must be clear that the experiments are no more than a test of the already well-tested special relativity, and of the principle of equivalence, and are therefore not to be compared for interest with others, such as those of Weber, which are a severe test of relativity theory. Indeed one would be hard put to devise any Lorentz-invariant theory of space-time which disagreed with the results of Hafele and Keating.

Let I be an inertial frame with respect to which the metric of flat space-time, in cylindrical polar coordinates, is

$$ds^2 = -c^{-2}(dz^2 + dr^2 + r^2 d\phi^2) + dt^2 \quad (1)$$

Number the coordinates $x^1 = z$, $x^2 = r$, $x^3 = \phi$, $x^4 = t$. Suppose we have two observers X and Y, such that X remains at rest at $(0, a, 0)$, and Y describes a circle, centre the origin and radius a , with angular velocity ω , relative to I. The world lines of the observers may be taken as

$$C_X : (0, a, 0, u) \quad C_Y : (0, a, \omega v, v)$$

where u and v are parameters, to be normalized so that the four velocities of X and Y satisfy

$$g_{ik} \frac{dx^i}{ds} \frac{dx^k}{ds} = 1$$

along C_X and C_Y , g_{ik} being the metric tensor of (1).

Our experiment takes place between two events A and B, at both of which both observers are present, namely

$$A : (0, a, 0, 0) \quad B : (0, a, 2\pi, 2\pi/\omega)$$

which are the start and finish of a circuit by Y. The intervals between them, as found by the two observers, are

$$s_X = \int_A^B \left(\frac{ds}{du} \right) du \quad (\text{evaluated along } C_X) = \int_0^{2\pi/\omega} du \quad (2)$$

$$s_Y = \int_A^B \left(\frac{ds}{dv} \right) dv \quad (\text{evaluated along } C_Y) = \int_0^{2\pi/\omega} \left(1 - \frac{a^2 \omega^2}{c^2} \right)^{\frac{1}{2}} dv$$

so

$$s_X = 2\pi/\omega \quad s_Y = 2\pi \left(1 - \frac{a^2 \omega^2}{c^2} \right)^{\frac{1}{2}} \omega^{-1} \quad (3)$$

The intervals between A and B are different for the two observers, as is to be expected because X and Y take different paths in space-time between A and B. Thus X describes a straight line between them, and Y a four-dimensional helix. Because ds is not a perfect differential, integrals such as those in (2) are path-dependent, and there is no reason whatever why they should be equal just because they have the same end-points.

So far we have done only mathematics. We put the physics in, and make contact with experiment, by the assumption that if the observers X and Y carry standard clocks, these will read the intervals s_X , s_Y . Hafele and Keating, and indeed most other writers, seem to take this more or less for granted. Now it is reasonable to suppose that standard clocks, when falling freely, record the interval, but if a standard clock is subjected to forces (like Y's), it is not at all obvious that it will do so. It is well known that subjecting clocks to forces sometimes has a pronounced effect on them—for example, if dropped on a hard floor they may break. Thus it is a definite assumption that a clock such as Y's, accelerated with respect to an inertial frame, records the interval. It seems to me that the most important contribution of Hafele and Keating's experiments is in the evidence they indirectly present that atomic clocks subject to the forces necessary to keep them in orbit in a jet plane continue to record the interval, or at least to record it as well as the Earth-bound clocks.

The formulae (3) form a theoretical basis for the interpretation of Hafele and Keating's experiments, but they need to be amended somewhat. In their experiments the terminal events are not A and B, but two events on the world line of a place on the rotating Earth. Moreover a gravitational red-shift term arises because of the height h of the flying clock above the Earth. Up to order c^{-2} , Hafele and Keating's formula for a clock in an equatorial orbit is

$$\Delta\tau \equiv \tau - \tau_0 = \left[\frac{gh}{c^2} - \frac{2R\Omega v + v^2}{2c^2} \right] \tau_0 \quad (4)$$

where τ , τ_0 are the times recorded by the flying and ground clocks, R , Ω the radius and angular velocity of the Earth, and v the speed of the flying aircraft, counted positive in the easterly direction. The linear term in v depends on the direction of flight (that is, east or west). In detailed calculations (4) needs modification to take account of the actual path of the aircraft, which was not equatorial, and variations in its height.

The kinematical and gravitational terms in (4) turn out to be of the same order of magnitude. The total time differences for a flight round the Earth were as follows:

	$\Delta\tau$ (ns)	
	Eastward	Westward
Mean $\pm$ standard deviation	-59 ± 10	273 ± 7
Predicted $\pm$ estimated error	-40 ± 23	275 ± 21

The estimated errors (chiefly from flight data for the aircraft path) are discussed at length. Four clocks were used on each journey, and delicate adjustments to the raw data were needed to correct for the vagaries of the clocks. For example, no two caesium clocks keep precisely the same time, but show systematic rate differences. Further, the rate of a clock may suddenly change, more or less permanently.

The agreement between theory and experiment is most satisfactory. As the authors conclude, "there seems to be little basis for further arguments about whether clocks will indicate the same time after a round trip, for we find that they do not".—W.B.

COMPOSITE MATERIALS

Toughened Glass

from our Materials Science Correspondent

It is one of nature's little ironies that many materials of particularly high strength are of little use as constructional materials. Substances such as silica, hard glass, alumina and boron nitride have extremely strong chemical bonding and thus very high intrinsic strength as well as high softening temperatures, but are also so brittle that they cannot safely be used under large loads, except in pure compression; the risk of fracture by mechanical or thermal shock is unacceptably great. There are promising exceptions—notably silicon nitride (see *Nature*, **238**, 128; 1972)—but glass and ceramics have usually been disappointing as materials for the mechanical engineer. This is why recent attempts to toughen these materials are specially important.

Reinforcement of weak materials with strong and stiff fibres or whiskers is now well understood in the laboratory and engineers' wariness is gradually diminishing. In industrial practice, all such composites have to date been based on polymeric matrices, most work having been carried out on glass-fibre reinforced epoxy resin. Carbon fibre is also being used to reinforce resins, but carbon-fibre reinforcement of metals for high-temperature use is less promising because of chemical attack of the fibres.

The very recent development of a radically new way of making continuous monofilaments of sapphire (J. T. A. Pollock, *J. Mater. Sci.*, **7**, 631, 649, 787; 1972; G. F. Hurley, *ibid.*, 471) offers new prospects of making effective high-temperature composites based on metal matrices. Here the high strength of the filaments will simply be utilized and the metal matrix will serve merely as a binder to transfer

stress to the fibres and (because of its deformability) to inhibit the spread of cracks.

A rival strategy is to use a strong brittle matrix with strong brittle fibres, and to depend on the interaction between these two brittle constituents to generate toughness. This is the idea underlying recent work at Harwell on the reinforcement by carbon fibres of glass, alumina, magnesia and glass-ceramic (R. A. J. Sambell *et al.*, *ibid.*, 663, 676). Sambell and his colleagues prepared their materials by hot pressing, with either discontinuous fibres or aligned continuous fibres, up to 40 per cent volume fraction. Substantial increases in bend-strength were recorded with the continuous fibres but there were variable results with discontinuous fibres. The fracture toughness, however, increases for all matrices and all fibre arrangements; in the most favourable combinations the increase in the work of fracture was more than a thousand-fold. For discontinuous fibres, the work of fracture increased with fibre content up to 30 per cent; beyond this, no further benefit was normally obtained. For continuous fibres, however, a sharp increase in work of fracture came at about 50 per cent volume fraction, provided the method of pressing used was designed to prevent excessive damage to the fibres. The results were best for glass matrices, least good for magnesia.

Sambell *et al.* discuss their very promising findings in terms, especially, of the mismatch of thermal expansion coefficients of matrix and fibres; this mismatch leads to internal stresses and for some matrices, especially magnesia, leads to matrix cracking during cooling from the hot-pressing temperature, and

such materials have relatively poor mechanical properties. Quite generally, however, matrix cracking occurred well before the ultimate tensile strength of the composite was reached.

Sambell *et al.* assume that the very high fracture toughness of some of their materials stems entirely from the work required to pull broken fibres out of the matrix, as cracks spread through the matrix. They ignore the work of fracture of the matrix itself, even though this must be far from negligible if the matrix is subject to multiple cracking. Sambell's analysis is cast in doubt by some work by G. A. Cooper and J. M. Sillwood of the National Physical Laboratory (*ibid.*, 325).

Cooper and Sillwood studied a model system consisting of epoxy resin reinforced with regularly spaced continuous steel wires of various diameters and volume fractions. The matrix was caused to crack in a very regular pattern by pre-cooling the composite in liquid nitrogen. This technique was adopted for simplicity in preference to mechanical testing which, however, led to similar cracking. For most composite samples, the observed crack spacings so created varied with fibre radius and volume fraction V_f in a highly regular way: the crack spacing was proportional to $(1 - V_f)/V_f$, and this is readily rationalized on the hypothesis that the critical fibre load-transfer length determines the crack spacing.

The really interesting feature, however, was the behaviour of samples with a high volume fraction of very fine wires. Such composites could not be cracked ahead of final failure, by either thermal or mechanical treatment. In an effort to understand this, Cooper

Different Haemoglobin Messengers

KAZAZIAN, in next Wednesday's *Nature New Biology* (August 9), shows that the rabbit haemoglobin messengers for α - and β -chains differ in size, and he has separated and identified the two species. In polyacrylamide gel electrophoresis, the 10S messenger RNA fraction gives rise to two bands of comparable intensity, which, it was surmised, were the two messengers. To verify this proposition, Kazazian introduced O-methylthreonine into the reticulocyte system. O-methylthreonine is an analogue of isoleucine, which blocks incorporation of this amino-acid into the haemoglobin chains. The disturbance results in the formation of large polysomes containing mainly nascent β -chains, whereas the α -chains, which contain isoleucine early in the sequence, are confined mostly to small polysomes.

Separation of these fractions and extraction of the messenger from each

revealed that the component of lower electrophoretic mobility was reinforced in preparation from β -chain polysomes, and the higher mobility species in those from α -chain polysomes. The difference in mobility seems to be truly related to molecular weight, for it persists when the base pairing is destroyed by formaldehyde treatment.

The calculated corresponding difference in size is somewhat bigger than would be expected in terms of the 5 per cent or so difference in the molecular weights of the α - and β -chains. Two bands are also observed in reticulocyte systems of other species. Kazazian has confirmed the result by using haemoglobin messenger from anaemic sheep of a genetic variant that synthesizes a third kind of chain in these conditions. This chain resembles the normal α - rather than the β -chain in molecular weight.

and Sillwood worked out a Griffith-type energy equation, relating externally provided work to the total internal energy release, by fibre stretching, matrix cracking and frictional resistance to fibre withdrawal. Their equations show that for a high volume fraction of fine fibres, there is indeed insufficient external energy available to sustain cracking of the matrix. They point out that their equations allow a composite to be designed so that matrix cracking and fibre fracture initiate simultaneously instead of sequentially. The matrix will then not begin to crack until the normal breaking strain of the matrix is reached, but (because of the need to pull out the simultaneously breaking fibres) the toughness will be much higher than for the unreinforced matrix. It seems probable that the sudden sharp increase of work of fracture of a glass matrix observed by Sambell *et al.* as they increased the volume fraction of aligned carbon fibre to 50 per cent is to be understood in terms of Cooper and Sillwood's theory: the sudden increase may well correspond to the critical situation outlined earlier.

The glass/carbon and ceramic/carbon composites studied at Harwell maintained their strengths at high temperature if tested in an inert atmosphere, but lost strength in air because the fibres oxidized. The chemical reactivity of carbon fibres, which limits their use in hot metal matrices, is thus seen to limit their usefulness in glass and ceramics also; but it may be that methods can be found to protect the fibres against oxidation, or else perhaps useful scope will be found for the composites in non-oxidizing atmospheres.

ENZYMES

Where the Action Is

from our Molecular Biology Correspondent
THE most casual perusal of the biochemical literature, as month follows month, is sufficient to reveal that the gnomes of the X-ray world have not been idle. The rows of coordinates, transferred from computer to the printed page, and the dispiriting sequences of minute stereograms, act, it must be said, as a powerful antidote to curiosity about the contents of the articles. To enzymologists and others, however, it is ultimately impossible to avoid the attempt at assimilation, and a series of articles in the current literature about chymotrypsin and subtilisin BPN', and their complexes with inhibitors, if resolutely approached, yield results of great importance and interest.

The most readable of these articles comes from Kraut's laboratory (Robertus *et al.*, *Biochemistry*, **11**, 2439 ;

1972), and concerns the interaction of subtilisin BPN with a series of peptide derivatives. These are in fact substrates, which attach covalently by way of a terminal alkylating group to the active site histidine residue, his-64. By applying the difference-Fourier method, the stereochemistry of the interaction of the peptides with the enzyme can be defined, and this is especially interesting in the case of a series of substrates of different sequence and length, which permit one to map the secondary specificity sites—the subsites—that interact with residues of the substrate other than that at which the scission occurs.

The difference maps for complexes with tripeptide derivatives in fact reveal the substrate as an extended chain, covalently fastened at one end to his-64; the terminal phenylalanine side chain, in accordance with the specificity of the enzyme, occupies the primary interaction site, which is in the form of a

crevice. The rest of the substrate chain is hydrogen-bonded to residues in the protein in an antiparallel β -fold arrangement. The his-64 side chain is evidently twisted about both the α - β and β - γ carbon bonds compared with its configuration in the free enzyme. There is evidence of some distension of the crevice to make room for the phenylalanine ring, which also displaces a water molecule. The corresponding peptide NH group makes a hydrogen bond to a backbone carbonyl in the protein, again with displacement of water. A less demanding interaction occurs at the second subsite, with some van der Waals contacts between hydrophobic side chains of the enzyme and substrate. The third site involves two inter-backbone hydrogen bonds, water being once more displaced. The fourth subsite, the existence of which is firmly established by earlier rate studies on a series of peptide substrates, is evidently a deep cavity, lined with several hydro-

Blocking of Cytotoxic Lymphocytes

THE notion that tumour cell populations in the living animal elicit from their host an immune response which can be both antipathetic to the tumour (the cellular component) and protective (the humoral component) is widespread and much discussed. The merit of the idea—for which there is considerable evidence chiefly from *in vitro* tests—is its simplicity and the direction it gives to immunologists who seek to manipulate the response to the advantage of the host. Attempts are being made to define the exact nature of the two components of the response, and in next Wednesday's *Nature New Biology* (August 9) R. W. Baldwin, M. R. Price and R. A. Robins present experiments which show that, *in vitro*, antigen-complexes can reduce cytotoxic effects of sensitized lymphocytes.

Baldwin *et al.* show that some cells of an aminoazo dye induced rat hepatoma, grown *in vitro*, can be killed by the addition of normal or sensitized lymph node cells. The sensitized cells kill about 40 per cent more tumour cells than do the unsensitized, but in all instances at least 15 per cent of tumour cells are left apparently intact. But in spite of the unexplained killing effect of normal cells and the lack of absolute efficiency on the part of the sensitized cells (a target cell: lymph node cell ratio of 1:2500 is used), Baldwin *et al.* conclude that their system is suitable for further study.

They go on to show the effect of adding normal serum, serum from rats taken 12–14 days after surgical removal of a tumour (post-excision—PE) and serum from tumour bearing rats. Only the last of these had the effect of blocking the attack by sensitized lymph node

cells. It had no effect on the cytotoxicity of unsensitized lymphocytes. Baldwin *et al.* show that addition of a soluble tumour extract which contains at least some of the tumour antigens to PE sera elicited a blocking capability. The amount of antigen added, however, was critical; large amounts of antigen were ineffective. Baldwin *et al.* conclude from this experiment that antibody is present in PE serum which itself cannot block but that when combined with appropriate amounts of antigen the formed complexes can become bound to the surfaces of the tumour cells and somehow prevent the attack of specifically sensitized lymphocytes.

The blocking effect of serum from tumour bearing animals was much reduced by the addition of large amounts of antigen. Baldwin *et al.* conclude from this and the previous experiment that some uncombined sites on the antibody component of the antigen-antibody complex are a prerequisite of successful blocking. Presumably it is envisaged that the blocking requires combination of the complex with the target cell surface and this needs free antibody combining sites.

Baldwin *et al.* point out that if their experiments bear any relationship to events in the tumour-bearing animal, injection of large amounts of purified antigen might well reduce blocking of cytotoxic lymphocytes by interfering with further deposition of the blocking complexes. If, as they hint, however, blocking may be in part mediated by alteration of the surface of the cytotoxic cells themselves (say by antigen) then the device may prove of no avail.

phobic residues, which, in the complexes with benzyloxycarbonyl-substituted tripeptides, accommodates this aromatic function, a tyrosine at the bottom of the cavity being twisted to make planar contact with it.

The rather irregular nature of the cleft at the first site explains in principle the relatively low specificity of the subtilisin, compared with chymotrypsin, for it can evidently accept leucine side chain, for example, as well as something aromatic. Other differences in the efficacy of inhibitors on the two enzymes have also been rationalized in specific steric terms. Beyond these results, which give stereochemical substance to a series of catalytic phenomena, lies an engrossing observation, however. A comparison with the structure of a complex of a similar peptide substrate with γ -chymotrypsin shows a quite extraordinary geometrical similarity. This embraces the β -sheet interaction and the nature of all the subsites. For purposes of quantitative comparison, the relevant segments of the two structures were extracted and brought into best-fit register by rotation. The result was a superimposition with a mean error of less than 1 Å, and a maximum deviation of only 2 Å at one point. The sites then are to all intents identical.

To appreciate the singular message of this finding, one must recall that in overall conformational terms, as well as in sequence, the two proteins are utterly unrelated: subtilisin, for example, has four times as much α -helical conformation as chymotrypsin, and contains parallel β -folds, whereas chymotrypsin has only some antiparallel regions. This then is by far the most conclusive example yet of convergent evolution, for it is scarcely arguable that two such different structures would have a common origin. One may pick out, in the subtilisin active site, the "charge-relay" system, which Blow discovered in chymotrypsin, involving the very same set of six residues, placed, albeit, quite differently in the primary structure.

The similarity between subtilisin BPN' and chymotrypsin (referred this time to the α -form) has been pondered also by Wright (*J. Mol. Biol.*, **67**, 151; 1972) and set out at some length. Wright notes first the identical juxtaposition of the catalytically important side chains in the two proteins, and goes on to compare the complexes of subtilisin with benzoylarginine (non-covalent) and chymotrypsin with formyltryptophan. The relation between the carboxyl groups on the inhibitors and the active site residues is again closely similar in the two cases. Wright's further thesis, however, concerns the primary specificity site, which in chymotrypsin is the well-defined "tosyl hole". The sugges-

tion is that in subtilisin two alternative primary specificity sites are available, and are utilized according to the nature of the substrate: acylating agents and competitive inhibitors bind at a different site from that for peptide chloromethylketone derivatives, for example. The interactions involved are defined on the basis of the known structures of enzyme-inhibitor complexes.

For technical reasons chymotrypsin has never in fact been crystallographically studied in conditions near the activating optimum. A chemical approach to the exploration of the size and shape of the active site has been attempted by Pattabiraman and Lawson (*J. Biol. Chem.*, **247**, 3029; 1972), using a series of locked, rigid, synthetic substrates, and deducing from the activities where any part of the substrate comes up against an obstruction in the enzyme. It is consistent with earlier inferences from the same kind of experiments that the primary binding site is a curved planar channel.

The definitive account by Birktoft and Blow of the tosyl- α -chymotrypsin structure at 2 Å has now appeared (*J. Mol. Biol.*, **68**, 187; 1972). The general features are familiar from the earlier accounts, but the new article contains a mass of analytical data which protein chemists will be eager to digest.

An interesting *bonne bouche*, that one might single out, is that practically all atoms capable of forming hydrogen bonds are so engaged, even in the interior of the molecule, some being bonded to other points in the chain, others to sequestered water molecules inside the structure.

NUCLEIC ACIDS

Primers and Templates

from our Cell Biology Correspondent

IN the good old days RNA and DNA and the polymerases which synthesize them were thought always to know their respective stations in life. DNA, the stable repository of genetic information, was believed always to be self replicated by DNA polymerase and RNA, the disposable copy of DNA, was supposed to always be copied from DNA templates and never the reverse. Viruses which have an RNA genome seemed easily to fit into this scheme of things because they appeared to have totally dispensed with DNA. The discovery of polymerases, first in RNA tumour viruses and subsequently in cells, which are able to use single stranded RNA as a template for the synthesis of double stranded DNA shattered this cosy scheme. The battered remnants which survived this first shock

Tracking Down Microbaroms

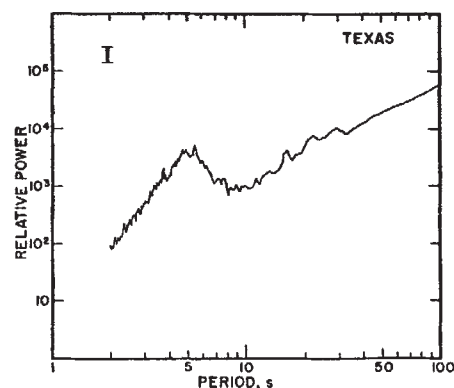
THE results of part of an Anglo-American programme for investigating the many kinds of infrasonic signals that make up the noise background against which explosions in the atmosphere have to be detected are presented in *Nature Physical Science* next Monday (August 7) by J. A. McDonald and E. Herrin of the Dallas Geophysical Laboratory.

McDonald and Herrin were particularly concerned with the so-called microbaroms, atmospheric noise signals with periods of about 5 s. These phenomena have been known for more than thirty years and among the mechanisms that have been suggested to account for them is one that has also been invoked to explain microseisms—standing water waves formed during marine storms.

In the experiments described by McDonald and Herrin three arrays of microbarographs in Alaska, England and Texas were used to detect the noise background. Data from one of the microbarographs in the Texas array for part of November 1971 had the spectrum shown here. The microbarom peak extends from periods of about 4 s to about 7 s. Measurements made with each of the arrays in late 1971 and early 1972, under atmospherically calm

local conditions, revealed microbaroms for which a possible oceanic source, usually in a low pressure area, could be picked out.

A subsidiary experiment with a smaller array in Texas, for which the microbarograph spacings were 0.2 km rather than 5 km as in the array proper, showed that there was significant coherence between signals from a pair of detectors in the small array but not between a pair in the large array. The coherence measurements were in accord with theoretical expectations, and McDonald and Herrin say that more experiments are planned using arrays with sensors spaced between a few hundred metres and 2 km apart.



have since fallen to the discovery that short RNA chains can *in vitro* and may *in vivo* act as primers for the self replication of double and single stranded DNAs by DNA polymerases which elongate DNA chains in the 5'-3' direction, polymerizing deoxy nucleotide triphosphates onto 3' hydroxy groups of primers.

The existence of RNA dependent DNA polymerases (reverse transcriptases) which can use RNA templates to make DNA was, of course, predicted by Temin to account for the curious biology of the RNA tumour viruses, but their potential usefulness to cells as well as these viruses is obvious enough; such enzymes, for example, provide, in theory at least, a way of amplifying any particular gene of which the RNA product of transcription is available. The classic example of gene amplification is the amplification of the ribosomal RNA genes during oogenesis in Amphibia and some insects, and as Crippa and Tochini-Valentini were quick to show in *Xenopus* oocytes this particular amplification is inhibited by a derivative of rifampicin, AF/ABDMP, which also inhibits the reverse transcriptase of RNA tumour viruses.

Both Crippa and Tochini-Valentini are clearly still enamoured of the idea that amplification of the ribosomal RNA genes depends on reverse transcription and with good reason, for Brown and Tochini-Valentini (*Proc. US Nat. Acad. Sci.*, **69**, 1746; 1972) have isolated from the ovaries of tadpoles in metamorphosis newly synthesized ribosomal DNA complexed with a transcript of the ribosomal RNA genes such that the sedimentation of the DNA is sensitive to RNAase. They have also shown that the RNA moiety of this complex can be used as a template for DNA synthesis by a DNA polymerase endogenous to the *Xenopus* cells in a reaction which is sensitive to AF/ABDMP. At the same time Mahdavi and Crippa (*ibid.*, 1749) have also isolated this ribosomal DNA ribosomal RNA complex and point out that the RNA fraction contains not only the mature 18S and 28S ribosomal RNA sequences but also the so-called spacer sequence which links these two genes but is not transcribed by RNA polymerase. All these observations constitute compelling if circumstantial evidence for the claim that ribosomal RNA genes in *Xenopus* are amplified by reverse transcription.

But irrespective of whether RNA chains have a template function during gene amplification, evidence that short RNA chains act as primers for DNA self replication in microorganisms is fast accumulating in several quarters. For one thing DNA replication in *Escherichia coli* seems to be sensitive to inhibitors of transcription, and as

Keller has recently shown *in vitro* at least RNA can prime the synthesis of ϕ X174 DNA. Now Sugino, Hirose and Okazaki (*ibid.*, 1863) have entered the lists by showing that the small strands of DNA—the famous Okazaki pieces which are made when *E. coli* cells are fed very short pulses of ^3H -thymidine—have a buoyant density in caesium sulphate greater than that expected of single stranded DNA. This and other observations lead Sugino *et al.* to the conclusion that Okazaki pieces, precursors of the nascent daughter DNA strands, are synthesized on RNA primer chains so that at early times they comprise covalently linked RNA-DNA; the RNA primer is presumably digested before the short DNA strand is ligated to the nascent chain.

Baltimore and his colleagues reported, of course, last year that reverse transcriptase from tumour viruses initiates the synthesis of DNA on RNA templates at the 3' hydroxy terminus of an RNA primer. The odds on very short RNA chains being universal primers of all DNA synthesis (except repair synthesis), irrespective of the nature of the template strand, are clearly shortening.

POPULATION ECOLOGY

Reproductive Strategies

from a Correspondent

CHARLES DARWIN observed that some insects lay many eggs and others but a few, yet this does not seem to be related to their abundance as adults. Ecologists are still attempting to develop a general theory broad enough to explain why some organisms devote a

higher proportion of their energy and material to reproduction than do others. This balance between allocation of resources to reproductive functions and to maintenance of the adult organism is one component of the organism's reproductive strategy. It is discussed in detail by Gadgil and Solbrig (*Amer. Nat.*, **106**, 14; 1972) who account for genetically based differences in this balance between three populations of dandelions (*Taraxacum officinale*).

MacArthur and Wilson (*The Theory of Island Biogeography*, Princeton University Press; 1967) have argued that, when a population is increasing in numbers and mortality is low, those genotypes which reproduce fastest will come to predominate. As the population approaches the carrying capacity (K) of its environment, set by resource limitation or by predation, mortality increases, along with selection pressures for characteristics favouring survival (predator avoidance strategies) or increased efficiency in exploiting limited resources (competitive ability). The response to these selection pressures in populations which remain for long periods close to the carrying capacity (K -selected populations) will be an increase in the proportion of resources devoted to increasing survival and efficiency, with a concomitant decrease in resources directly allocated to reproduction. In contrast, where repeated population extinction and recolonization occur, as in "fugitive" species characteristic of temporary habitats, selection for high rate of increase (r) in newly occupied habitats will favour greater allocation of resources to reproduction.

Gadgil and Solbrig use the generaliza-

Variability of DNA Content of *Bacillus* Species

In *Nature New Biology* next Wednesday (August 9) Johnston and Young report an investigation by electron-autoradiography of the amount of DNA in individual cells and spores of *Bacillus subtilis* and *B. cereus* and they conclude that in both cells and spores the amount of DNA is very variable. Estimates of the size of the genomes and DNA contents of *Bacillus* species are notoriously disparate and to obtain fairly accurate estimates of the amount of DNA in individual spores and cells Johnston and Young had to resort to a very laborious procedure.

They grew cells for ten to twelve generations in a medium containing ^3H -thymidine and then produced serial sections of labelled cells and spores and made micrographs which were projected and the silver grains were traced and then cut out. As calibration experiments with *Escherichia coli* revealed, the weight of the grain tracings

gives a fairly accurate estimate of the total DNA pre-cell or pre-spore.

When the amount of DNA in *Bacillus* cells and spores was estimated in this fashion three unexpected findings emerged; first the amount of DNA in different cells of the same species can vary by as much as four to five-fold; second, in individual cells the DNA in a spore is not always a constant fraction of the amount in the sporulating cell; third, the amount of DNA in spores is quite variable.

Johnston and Young estimate the genome of *B. cereus* to be 3×10^9 daltons in which case individual cells may contain from 5-20 genomes whereas spores may have 1-8 genomes, and *B. subtilis* cells may have from 2-9 genomes and *B. subtilis* spores 1-4 genomes. The biochemical basis and evolutionary significance of these striking variations are at present matters for speculation.

tion that predation and intraspecific competition are density-dependent factors, resulting in proportionally higher death rates or reduced reproduction at higher densities, and thereby determining the value of K . Where density-independent factors (such as climatic catastrophe) reduce population size below the carrying capacity, competition and predation are reduced, allowing a "compensatory" increase in numbers. The authors argue that, from the point of view of the organism, density-independent factors are less predictable in their nature and occurrence than are density-dependent ones. Because it is simpler to evolve mechanisms to deal with predictable events, organisms subject to high rates of density-dependent mortality will evolve such mechanisms and become K -strategists. Frequent density-independent mortality will favour r -strategists, both from the earlier argument and because such mortality, by keeping population density at levels below the carrying capacity, reduces selection pressures associated with predation and competition.

On this theme it is noted that reduction of competition and increase in resources per individual may automatically increase reproductive rates with no change in the proportion of resources allocated to reproduction. Thus, data showing variation of fecundity with habitat type may indicate variation in either resource availability or reproductive strategy.

Gadgil and Solbrig identified four dandelion "biotypes", each characterized by isozyme pattern as well as morphology, from three populations which differed in their biotype composition. Plants which are crowded compete with each other for soil nutrients and, by shading each other, for sunlight. In laboratory competition experiments in various soil and light conditions the "D" biotype consistently out-competed the "A" biotype. In non-competitive situations, each A plant produced three times as many seeds as each D plant. Comparison of dry weight ratios of reproductive to vegetative tissue showed that the A biotype was an r -strategist in relation to the D biotype. These results support the assumption that competitive and reproductive efficiencies cannot be simultaneously maximized. Furthermore, the result of the competition experiments suggests that differences in biotype composition of populations reflect selection acting not on microclimatic adaptations but on reproductive strategies. As the theory outlined here would predict, the frequency of A is highest in the population with most human interference (density-independent mortality) and that of D is highest in the least disturbed and most competitive situation.

NATURE CONSERVATION

Peatlands in the USSR

from our Plant Ecology Correspondent

THE conservation of habitats which have some amenity value for the public is now becoming commonplace, but the conservation of habitats which are of purely scientific interest is more difficult to justify. Peatland habitats suffer not only from this disadvantage but also their continued survival is further threatened because of their potential use in supplying peat for horticulture and power and in providing areas suitable for forestry.

There have been indications recently that the climate of opinion is beginning to change, and this fact became apparent at the fourth International Peat Congress held in Helsinki from June 25 to 30. This congress was organized by the International Peat Society, a body which in the past has been concerned chiefly with the exploitation of the world's peat resources, but is now showing an increasingly informed concern for the scientific conservation of representative peatland types. For example, four years ago at the third International Peat Congress held in Quebec, only two communications were concerned with conservation; at the Helsinki congress an entire section was given over to problems of peatland conservation.

From this section came welcome news of peatland conservation projects in the

Soviet Union. About one tenth (approximately 71.5 million hectares) of the total land area of the Soviet Union is peatland and this nation has a long-standing reputation for the efficient exploitation of these resources: indeed 87 per cent of the world's peat production takes place in the Soviet Union. But in spite of this emphasis on exploitation peatland nature reserves in the Soviet Union are not entirely a new feature, for the Astrakhan State Nature Reserve, a 400 km² area of peatland in the Volga delta, was in existence in 1919. Now, according to Professor Viktor Masing (Tartu State University), there are eighty such state nature reserves (zapovedniks) in the Soviet Union, and many of these contain peatland areas.

Justification of peatland conservation in the Soviet Union is based on a number of considerations. In the first place, scientific value receives a high rating, though much emphasis is still placed on the protection of locally endangered species, some of which—for example, *Erica tetralix*—would hardly merit such concern in Europe outside the Soviet Union. Selection of conservation areas on this criterion must take into consideration the international status of the species concerned. Economic considerations, such as the use of extensive mire systems for water conservation and for cultivating plants such as *Oxycoccus palustris* and *Rubus chamaemorus* (both used for the manufacture of liqueurs),

Mammary Tumour Viruses

SOME inbred strains of mice have a high incidence of mammary tumours whereas others rarely develop this disease. In at least some of the high incidence strains mouse mammary tumour virus, the causative agent, is transmitted horizontally in milk whereas in the GR high incidence strain it is transmitted vertically in both male and female gametes as a simple autosomal dominant; presumably a DNA mouse mammary tumour provirus(es) is part of the genome of this strain. But what is the situation in the low incidence strains? Do they contain such proviruses but fail to express them or do they lack the provirus?

According to the results of hybridization experiments with mouse mammary tumour virus DNA and cell DNA, which are reported in *Nature New Biology* next Wednesday (August 9) by Varmus and his associates, both GR high incidence mice and C57Black low incidence mice contain perhaps as many as ninety mouse mammary tumour proviruses per genome, from which it follows that the phenotypic differences in incidence of mammary tumours between these

two strains must result from differences in regulatory genes which they carry and which control the expression of mouse mammary tumour virus DNA.

This finding is in line with reports of Varmus *et al.* and others who have detected Rous sarcoma virus sequences in healthy chick cell DNA, and murine leukaemia virus sequences in normal mouse cells. Together these observations indicate that the vertical inheritance of mouse leukaemia virus, mouse mammary tumour virus and Rous sarcoma virus DNAs is probably widespread in mice and chickens, the respective host species.

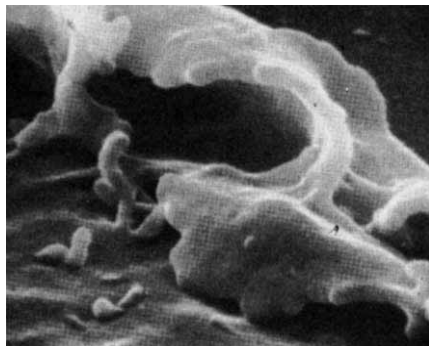
Two years ago Chopra detected an RNA virus, M-PMV, in a spontaneous breast tumour of a rhesus monkey and also in next week's *Nature New Biology* Fine and six colleagues, including Chopra, report that when this agent is inoculated into newborn female *Macaca mulatta* monkeys it proliferates in the animals' lymph nodes. The virus has also recently been shown to transform cultivated rhesus monkey cells and so the odds on this virus being carcinogenic for the rhesus monkey are fast shortening.

are also important. Furthermore, the Russians would seem to appreciate the recreational potential of peatlands to a far greater extent than do the British.

MEMBRANES

Ruffling Enlarged

ELECTRON micrographs of biological material are now commonplace in the literature but they rarely fail to be fascinating aesthetically quite apart, of course, from the fact that they convey interesting information. This picture of a ruffling membrane of monkey kidney cells in culture was obtained by Dr Z. H. Price of the University of California and complements three-dimensional models which Price constructed by assembling enlarged 'Styroform' duplicates of serial sections of the cells (*J. Microscopy*, **95**, 493; 1972).



Scanning electron micrograph showing the formation of endocytotoxic vesicles by the collapse and coalescence of processes with the cell membrane. Microvilli are present on the surface of the cell. $\times 14,850$.

A ruffling or undulating membrane is a phenomenon associated with the moving boundary of cells maintained on a solid surface. The phenomenon has often been observed in both the light and electron microscope but the activity is little understood, although it seems to be implicated in the locomotion and endocytosis of cultured cells. Price used the LLCMK₂ strain of monkey kidney cells because ruffling and endocytosis are particularly prominent on the multinucleate giant cells of this strain. The cells were examined by time-lapse cinematography and serial sections were cut at right angles to the plane of the substrate.

Price found from the models and scanning electron micrographs that the writhing movements of ruffling in LLCMK₂ cells were caused by the protrusion and subsequent collapse of processes from the membrane and ectoplasm originating along the margin of the cell. Most of the protrusions were flattened sheet-like extensions, but Price also noticed round, villus-like protrusions along the folds. Formation of the processes of ruffling seemed to occur at random.

An endocytotoxic vesicle was formed

when the descending tip of the process came into contact with the membrane (see figure). Time-lapse films of the cells clearly showed the movement of the vesicles from the areas of ruffling to the perinuclear region.

SOLAR SYSTEM

Assembling the Planets

THE process of accretion by which dust grains in the primitive solar system accumulated to form the planets, their satellites and other bodies has been examined experimentally by J. F. Kerridge and J. F. Vedder working at the NASA Ames Research Center. Their aim was to learn more about the range of impacting velocities between dust particles which will lead to accretion, and their results are reported in *Science* (**177**, 161; 1972). It is known that at the low relative velocities which must have existed throughout much of the cloud, colliding silicate particles would have stuck together, but colliding metallic particles are more likely to have rebounded. Kerridge and Vedder, however, have now examined the behaviour of colliding silicate particles for somewhat higher relative velocities.

Kerridge and Vedder used a 1.5 MV linear accelerator to accelerate charged flakes of silicate—which must have been the commonest type of dust particle in the early solar system—and the accelerated flakes struck a 1-cm² target also composed of a silicate. Impact velocities between 1.5 and 9.5 km s⁻¹ were achieved, and the silicate particles had masses between 0.2 and 120×10^{-12} g.

To discover to what extent the accelerated particles were being accreted on the target, Kerridge and Vedder used electron microprobe analysis to look for fragments of the

impacting material—kaolinite, Al₂O₃·2SiO₂·2H₂O—adhering to the chrysotile target (3MgO·2SiO₂·2H₂O).

They discovered, however, that at all the velocities studied erosion rather than accretion seemed to be occurring. Although fragments of the impacting material were sometimes found adhering to the target, these occasions were outnumbered by cases in which no impacting material could be detected on the target. And photographs of the target taken with a scanning electron microscope showed that the impacts were leaving craters comparable in size or even greater than the size of the impacting particle. Kerridge and Vedder doubt whether compression of the target material during impact could account for more than a small proportion of the size of the craters.

What implications does this negative result have for theories of the formation of the solar system? Kerridge and Vedder point out that in earlier experiments by G. Neukum using similar-sized particles and similar impact velocities, but using metallic particles rather than silicates, accretion was probably occurring for velocities from 0.5 km s⁻¹ to at least 1.5 km s⁻¹. But at lower velocities, which would have allowed colliding silicate particles to adhere, metallic particles simply rebounded from one another.

This difference between the behaviour of the two kinds of particles might have led to fractionation of the solar system material. At low relative velocities silicates would have accreted rather than metals, but at higher velocities metallic particles would have been favoured. In conclusion Kerridge and Vedder remark that there is a rough tendency among the terrestrial planets for density, and therefore presumably metal content, to increase with orbital velocity.

Structure of an "Enol" Nucleoside

Schwalbe, Gassen and Saenger, in next Wednesday's *Nature New Biology* (August 9), report the determination of the crystal structure of 3-deazauridine. This analogue differs from the normal nucleoside in having the N-H group, which forms one of the two hydrogen bonds in the Watson-Crick adenine-uracil base pair, replaced by C-H. Differences in the hydrogen bonding potentiality of 3-deazauridine as compared with uridine are, however, not confined to the 3 position of the ring.

X-ray analysis shows that in the crystal environment the base is in the keto-enol form rather than the double-keto form characteristic of uracil. The additional hydrogen in 3-deazauridine is bound to O₄, the oxygen attached to C₄ of the pyrimidine ring. This hydroxyl group is apparently a very

potent hydrogen bond donor because it forms a rather short hydrogen bond of 2.549 Å to the 2-keto oxygen of the pyrimidine residue in a neighbouring molecule. X-ray analysis shows that the hydrogen atom in this bond lies much closer to O₄ than to O₂, and is clearly not, as has been suggested for other very short O-H...O bonds, disposed symmetrically between the two oxygens.

Schwalbe *et al.* discuss the base pairing possibilities for 3-deazauridine in the light of their results. One point of interest is that the hydroxyl group at position 4 of the pyrimidine ring is not only a potential hydrogen bond donor in base pairing schemes but also, because of the possibility of free rotation about the C₄-OH single bond, can flip from being a donor to an acceptor in a particular direction.

World Dynamics : Social Feedback may give Hope for the Future

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"World Models", derived by system dynamics, are discussed. The wide uncertainty of these models makes pessimistic predictions by no means certain, and more hopeful predictions appear equally valid.

It is outside the scope of this article to give an explanation of the method used at MIT to produce the world models that have recently aroused much attention. We shall give an outline of the history and the interested reader can find details in the references.

In 1961 Professor Jay W. Forrester published his book *Industrial Dynamics*¹. As he writes in the preface, it presents a way of studying the dynamic behaviour of industrial systems *via* a model-building approach. The method has been designed specifically to study the behaviour of a system as it follows from the individual relations between the system components. Like most simulation methods it can best be applied to well-structured functional areas where the main variables are known and there is an insight into the interrelation processes^{2,3}.

Later Forrester applied the method not only to industrial but also to social systems⁴—for example, urban development⁵—and the name was changed to "System Dynamics". At about the same time the Club of Rome, an international group of scientists and industrialists who are worried about the growth trends in our finite world, wanted to start a project on the predicament of mankind. In 1970 it was decided that the System Dynamics technique would be used for this project.

The World-2 model⁶ is a tentative model used to demonstrate the suitability of System Dynamics for this project. The five main variables taken to represent the relevant state of the Earth and studied in their interconnexions in this

model are: population, capital investment, natural resources, pollution, and capital investment in agriculture. The model on which the report of the Club of Rome⁷ is based is called "World-3" and it has more extensive population, industry and agricultural sections than World-2.

Understandably, these publications have received much attention^{8,9} because of the subject dealt with and the pessimistic inferences. This attention is useful because the interest of a large public is an essential condition for possible intervention in the development of the world, should this be required. Moreover, as a result the people and money required for further research may now become available.

A study of the demographic and economic growth processes and their interactions on our "Spaceship Earth" is not only a challenging but also a very important project.

As far as we know System Dynamics has provided the first integral model of these phenomena and clearly it has something to offer in this respect. But we are faced with the important problem of evaluating these models to establish what justified conclusion about the real world can be drawn from the model studies, before we can base any policy decisions on them. This article is offered as a contribution to the discussion about this evaluation; we shall show that it is still too early for policy conclusions.

Criticisms of the MIT World Models

As early as December 1971, criticisms based on computer experience with the World-2 model were published¹⁰ under a few main headings. These were: First, lack of empirical content of the models. At least for chemical and physical processes one of the most important requirements to be placed on computer models is that the results should be verifiable. That is, output from model computations should be comparable with data that have been gathered from measurements on actual processes or during experiments. Only when this has been done may we attach any forecasting value to such models. Because of the highly aggregated character of the World-2 (and World-3) model this condition is not satisfied. With the exception of the population level, the variables are

non-empirical and therefore cannot be verified. For instance, who can say what the height of the 1970 global pollution level—which in the model is meant to be a measure of the world-wide effect of environmental disruption caused by man—should be in relation to the 1900 level?

Second, lack of insight about system structure. As in many social systems it is questionable whether we can indicate

Dynamics is a valuable technique which may provide considerable insight.

Here we demonstrate ways by which the objection to the lack of a social feedback mentioned in ref. 10 can be removed while using the System Dynamics technique. We do this by introducing a feedback loop on the pollution level. Furthermore, we have made the dragging effect on the depletion of

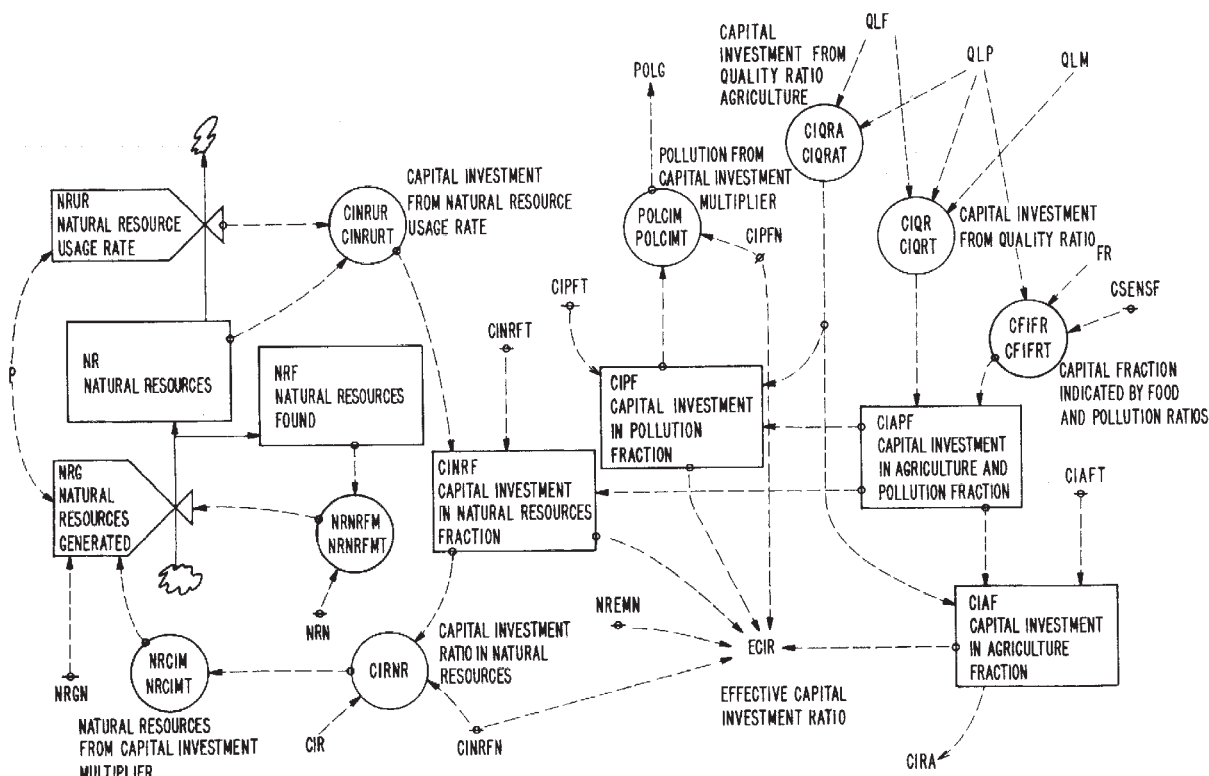


Fig. 1 Extension of "World-2" model.

the variables and relations that determine the behaviour of the demographic and economic systems of the world. In physics or chemistry we usually have a theoretical back-up of a model structure and quantitative relations can be verified with experiments. Many functional relationships are used in the MIT world models for which we have no theory, evidence or experience.

Third, model sensitivity. The above-mentioned problems are the more serious because, as has been confirmed by our in-house simulations, the model results are highly sensitive to small variations in some input functions and parameters in the capital investment, resources and pollution sections of the World-2 model.

Four, lack of social feedback. The model structure does not leave sufficient scope for mankind to intervene when the world system develops in an undesirable direction. We shall revert to this below.

Other criticisms concern the entirely deterministic nature of the models and the supposed reversibility of all model relations. We are aware that we should be very careful with reactions of disbelief because these may shield us from the pessimistic inferences. Nevertheless we consider that much multidisciplinary research is required before a model can be developed on which policy decisions can be based. After all, some forecasting value is required if we want to be able to draw policy conclusions, and in such work System

natural resources more explicit, thereby increasing the empirical content of this part of the model. Of course, the above-mentioned criticisms against the model still hold against our modified version. We do not suggest our augmented model is a better one, with a higher forecasting value, but our results show that, using System Dynamics, one can construct a much more stable future outlook, which is less prone to crises than the World-2 and 3 models. This will demonstrate our point that more research is required to enable us to gain a good insight into our future.

Feedback to Prevent Pollution

Discussing the relation in World-2 between the Capital Investment Ratio and Pollution Generation, Forrester⁶ writes: "... if the high levels of capital investment imply capital devoted to pollution control, the pollution might no longer rise with increasing capital investment". For a well-functioning feedback such control is imposed, not at a high level of capital investment, but rather when the pollution itself becomes (too) high. At the moment such an extra feedback is already clearly noticeable in legislative action, particularly in the USA, but also in North-West Europe. Political and social pressures are building up.

In the World-2 model Professor Forrester gives one example of this type of feedback: the Capital Investment in Agriculture Fraction (CIAF) is determined by the Food Ratio

(FR) and the ratio of Quality of Life from Material to that from Food. If there is relatively little food and, at the same time, a high Material Standard of Living (MSL), relatively more will be invested in agriculture. We have built into the World-2 model an analogous control mechanism for pollution.

At present, money is already being spent on measures for environmental preservation. Sewage installations form an example; motor cars can be equipped with installations which drastically reduce the percentage of noxious components in the exhaust gases, but at certain extra costs. This holds much more generally and the possibility of reducing pollution generation at a cost seems a very realistic one. It is evident that the precise relation between the percentage reduction and its cost depends on the nature of the measures taken and can only be determined with the aid of a considerable amount of research. The relations used by us are purely intuitive.

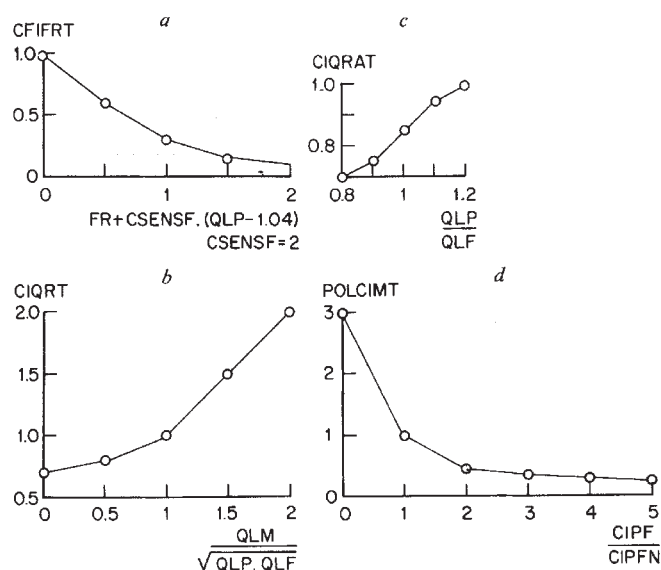


Fig. 2 *a*, Desired capital fraction invested in agriculture and in pollution control as a function of the Food Ratio and the Quality of Life from pollution. *b*, This relationship keeps a reasonable balance between QLM on the one side and QLP and QLF on the other side. The CIAPF is changed, when unbalance would occur. *c*, Split between fraction of capital invested in agriculture and that in pollution control as a function of the QLP/QLF ratio. *d*, Effectiveness from capital fraction invested in pollution control.

The extension to the World-2 model which we have been running on a computer is shown in Fig. 1. The terminology is based on Forrester's⁶. First, the total fraction of investment in agriculture and pollution control together (CIAPF) is determined. This is done via the tables CIQRT and CRIFRT (as in the original model), but we have modified the abscissa FR and the quality ratio QLM/QLF with the Quality of Life from Pollution QLP (Fig. 2*a* and *b*). Depending on the ratio QLF/QLP (Fig. 2*c*) CIAPF is split up into a Capital Investment in Agriculture Fraction and a Capital Investment in Pollution Fraction. The efficiency of investment in pollution control is described by multiplying the Pollution Generation by the Pollution from Capital Investment Multiplier (Fig. 2*d*). This multiplier is a non-linear function of the investment fraction accounting for the decreasing marginal effectiveness when the investment fraction increases considerably above its 1970 value. The computer data and 1970 levels are shown in Table 1.

Making the Natural Resources Section More Explicit

The World-2 and World-3 models work with a fixed level of non-replaceable resources, which can only decrease. This implies that this level must incorporate all materials that could possibly ever be used as a resource, from now to the end of the world. Therefore, the interpretation of what is a

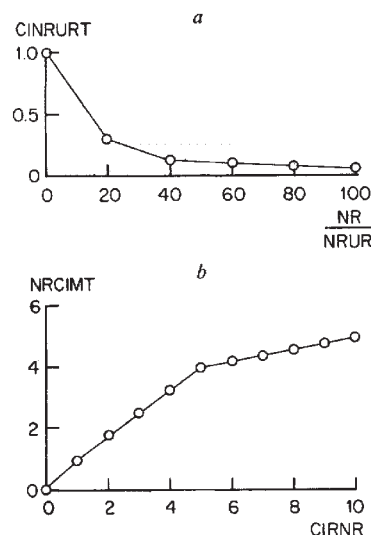


Fig. 3 *a*, Influence of static reserve life index on the fraction of capital invested in the generation of natural resources. *b*, Decreasing incremental yields from capital invested in the search for natural resources

natural resource, and hence, how much of it exists, becomes very difficult. One may wonder whether uranium was a resource in 1900 and what things not at present thought of as resources will become resources before the year 2100. Moreover, man may well be able to increase the ultimately recoverable amount of, for instance, oil or metals by investing money in exploration.

With regard to the non-replaceability, if ever we could re-

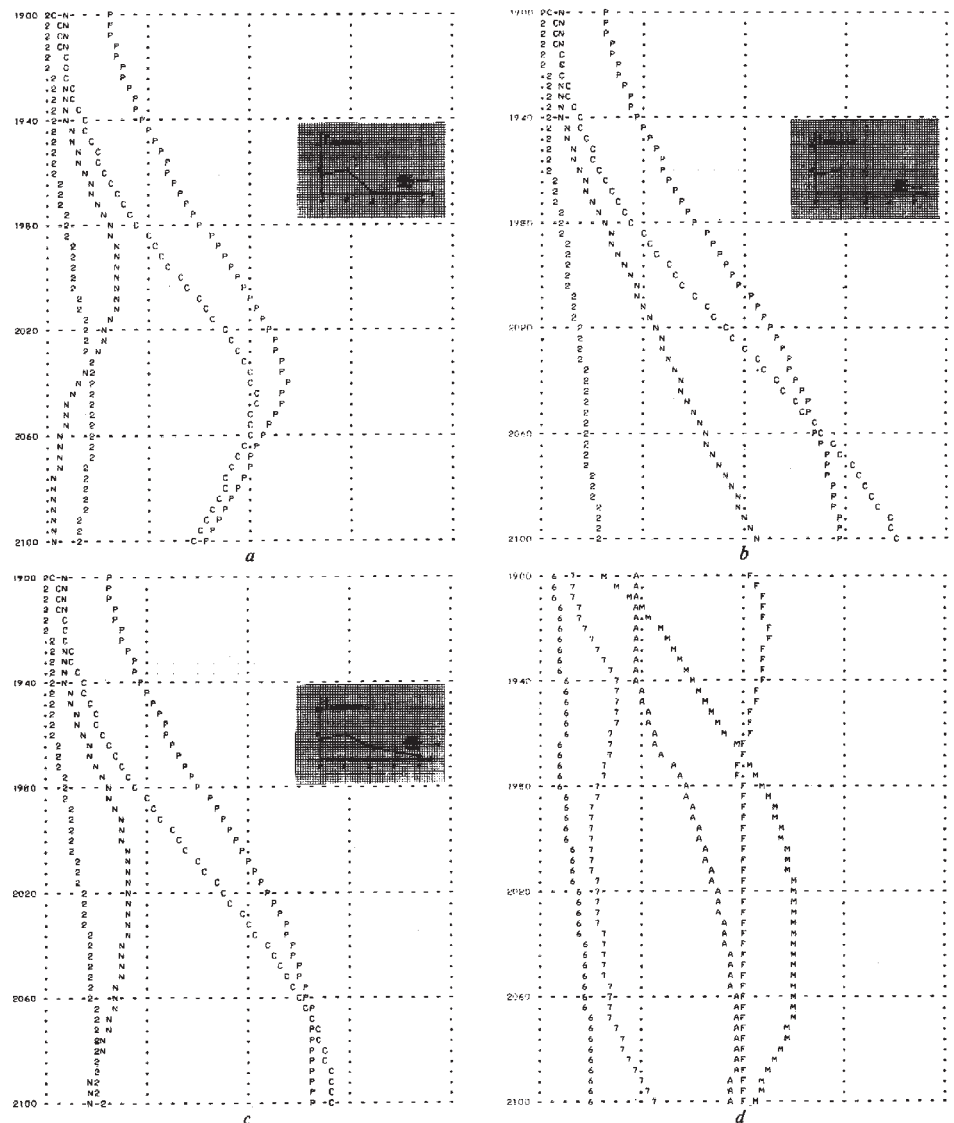
Table 1 Explanation of Computer Output

Symbol	Name in model	Description	Value in 1970	Scale
P	P	Population	3.6×10^9	0- 10^{10}
C	CI	Capital investment	3.6×10^9	0- 2×10^{10}
N	NR	Natural resources usage rate in 1970	14.5×10^{10} 3.6×10^9	0- 10^{12}
2	POLR	Pollution divided by 1970 pollution	1	0-40
A	CIAPF	Capital investment in agriculture fraction	0.3	0-0.8
6	CIPF	Capital investment in pollution fraction	0.05	0-0.8
7	CINRF	Capital investment in natural resources fraction	0.10	0-0.8
M	MSL	Material standard of living	1	0-2
F	FR	Food ratio	1	0-2

cycle, for instance, copper from scrap or invent a substitute material, what would this mean with regard to the quantity of resources according to Forrester and Meadows? In their models the Natural Resource Extraction Multiplier (NREM) ensures that the efficiency of investment decreases as resources are depleted. This may mean that it takes more and more money to extract the next, less economical, unit and that money invested in the extraction process does not contribute to the material standard of living and capital generation. It may also mean that ever more expensive exploration has to be carried out to discover yet more resources.

is determined via the table CINRURT (Figs. 1 and 3a). This is a plausible process but up to now it has probably been hidden by the development of technology, which has so far rendered a steep increase of investment in natural resources unnecessary. In this new set-up the momentary level of resources NR (Fig. 1) becomes a more readily recognizable quantity. This level is now defined as the momentary discovered and economically exploitable reserve of resources. Therefore, the initial value of this variable is about 1/20th of the amount of resources in 1900 in the World-2 model. The static reserve life index in the augmented model is about 40

Fig. 4 *a*, The World-2 "base case" from the augmented model. *b*, The future outlook resulting from constant opportunities for the creation of resources. *c*, The "intermediate" case. *d*, The "intermediate" case: capital fractions, material standard of living and food ratio. Forrester's "Quality of Life" has apparently disappeared from the "World-3" model. We also omit it because of its rather arbitrary definition. The Natural Resources curves naturally behave differently because of the change in definition of natural resources.



All these possibilities boil down to increasing the recoverable amount of resources at a cost. In the World-2 and World-3 models all such increments should be accounted for when setting the initial level. It is hard to recognize in these models the effect of capital allocated to any of the above possibilities to avoid a resources shortage.

Rather than via the table NREMT, which we have replaced by a constant, we have created the explicit opportunity to allocate money to increase the amount of resources by a feedback loop via the static reserve life index, that is, the number of years for which, on the basis of the present usage rate, economically recoverable resources exist. On the basis of this index the Capital Investment in Natural Resources Fraction

in 1970. Once the *per capita* investment in natural resources has been determined we must know how much resources this money is going to create. Our assumptions on this point can be found in the table NRCIMT (Fig. 3b). It shows the law of diminishing returns.

However, processes to find more resources or extract less economical ones become increasingly less effective as more have been found already and thus, in a sense, less remain. To incorporate this effect we have introduced an extra level, Natural Resources Found, which registers all resources found since 1900. As this level increases via the table NRNRFMT (the Natural Resources from Natural Resources Found Multiplier) increasingly hinders the generation of resources.

These tables have also been based on intuition. We shall demonstrate that varying the table NRNRFMT can produce a complete spectrum of prospects for the future and within this spectrum the World-2 base case can also be found. But we can now clarify the assumptions which Forrester has made when choosing the table for his NREM. On trying to realize a more optimistic outlook with the World-2 model, by increasing the NR level or changing the table NREMT, a pollution crisis follows. In our augmented model such a crisis is avoided through the feedback introduced.

Modified Models and Discussions

Various computer results and the related NRNRFMT tables are shown in Fig. 4. In Fig. 4a this table has been chosen to reconstruct the World-2 base case with reasonable accuracy. What is required is a very steep descent of the function for values of NRF larger than NRN (this is the 1970 value of NRF), for $\text{NRF}/\text{NRN} \geq 2$ NRNRFMT is practically zero. So, together with the rest of our assumptions, this suggests that Forrester has implicitly assumed that it is possible to find twice the amount found between 1900 and 1970, but hardly any more.

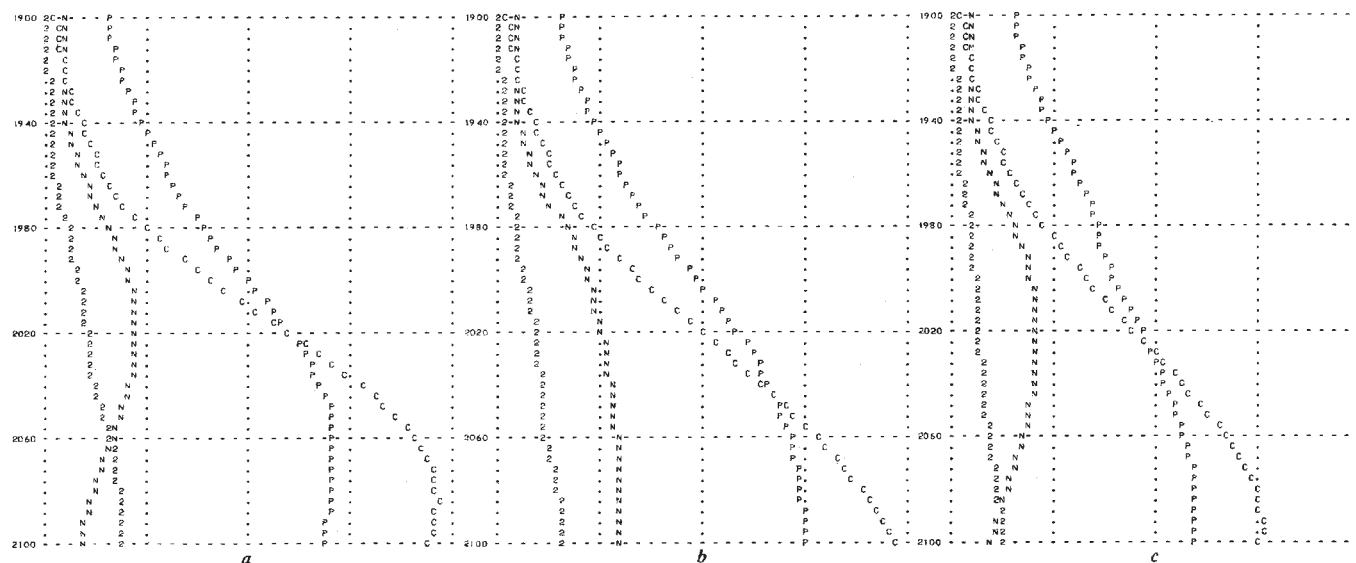


Fig. 5 a, Effect of increased capital investment generation from 1970 onwards. (CIGN 1 from 0.05 to 0.06) with 4c as a base case. b, Effect of reduced NR usage rate from 1970 onwards. With 4c as a base case (NRUN from 1 to 0.25). c, Effect of a reduced birth-rate from 1970 onwards. (BRN 1 from 0.04 to 0.028.)

Fig. 4b represents quite a different point of view. At any time in the future a certain amount of capital will find us with the same amount of resources as at present; increasing scarcity, depth, etc., would be offset by technological advances, as was apparently the case before 1970, as shown by the shape of the function NRNRFMT for values of NRF/NRN between 0 and 1. However, the law of diminishing returns as shown in Fig. 3b is still at work.

Fig. 4c shows an intermediate case, which is not necessarily the most likely one. It is interesting to note that, under these relatively moderate assumptions, the population level stabilizes and no dramatic effects occur before 2100. In Fig. 4d some other variables related to this case have been pictured. Among these are the capital investment fractions in agriculture, in pollution control and in natural resources.

Fig. 5 shows the results of changes in a number of important variables. The above intermediate case is taken as a base case. In Fig. 5a the Capital Investment Generation has been increased by 20% from 1970 onwards (CIGN 1 from

0.05 to 0.06). For the World-2 model this gives rise to a pollution crisis, which is now avoided by a reallocation of capital. What does occur is an increased use of natural resources.

In Fig. 5 the natural resources usage rate has been reduced by a factor of 4 in 1970. With the World-2 model this also leads to a pollution crisis; here it results in a prolonged industrial growth. A reduction in the birth rate (BRN from 0.04 to 0.028 from 1970 onwards) has only a limited influence on the population level and hardly any on the other levels (Fig. 5c).

A kind of social feedback which can already be seen active at present—an example is increased investment in pollution control—and which is not included in MIT's World-2 model, has a strongly stabilizing effect on its behaviour. This could justify environmental conservation legislation. The revision of the natural resources section increases the visibility of the contents of this section, and it becomes apparent that different but reasonable assumptions about future discoveries and the influence of technology on these can yield a spectrum of future outlooks that are not all *a priori* unattractive. The forecasting value of this model is still rather low and serious

scientific research is required before any final views can be justified.

We thank Dr M. H. Rothkopf of Shell International Petroleum Company for discussions and Mr D. P. de Graag (Kon/Shell Lab., Amsterdam) for the computer implementation.

- 1 Forrester, J. W., *Industrial Dynamics* (MIT Press, Cambridge, 1961).
- 2 Ansoff, H. I., and Slevin, D. P., *Management Sci.*, **14**, 7 (1968).
- 3 Forrester, J. W., *Management Sci.*, **14**, 9 (1968).
- 4 Forrester, J. W., *Simulation*, **2** (1971).
- 5 Forrester, J. W., *Urban Dynamics* (MIT Press, Cambridge, 1969).
- 6 Forrester, J. W., *World Dynamics* (Wright-Allen Press, Cambridge, 1971).
- 7 Meadows, D. L., et al., *The Limits to Growth, A Report on the Club of Rome's Project on the Predicament of Mankind* (Potomac Associates, New York, 1972).
- 8 *The Economist*, 20, March 11 (1971).
- 9 *Time*, 28, January 24 (1972).
- 10 van der Grinten, P. M. E. M., and de Jong, P. J., *Chemisch Weekblad*, **10** (1971).

Stardust

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Heavy metal particles have been detected in noctilucent clouds. Possible sources for these particles are considered and a solar origin is suggested.

DURING the summer of 1970 we carried out two rocket experiments to collect particles from noctilucent clouds at Kiruna, Sweden^{1,2}, and we found that approximately 70% of the collected particles consist of two components. Examination by electron microscope and electron beam probe suggested that the central component, which is of high density, contained a surprisingly large number of atoms of high atomic weight such as lanthanum, thulium, praseodymium, osmium, ytterbium, and tantalum. We describe here further work on these particles, based on the 1970 experiment and on two additional flights from Kiruna during the summer of 1971, again during a display of noctilucent clouds.

electron-opaque core surrounded by a rounded, low density material. Examples of particles without a low density coating are shown in Figs. 5 and 7. In the 1970 experiments, approximately 70% of the particles were of the two component type; in 1971, only about 15% were of this type. In both years the remaining particles were mostly single component, submicron irregular particles of high electron optical density.

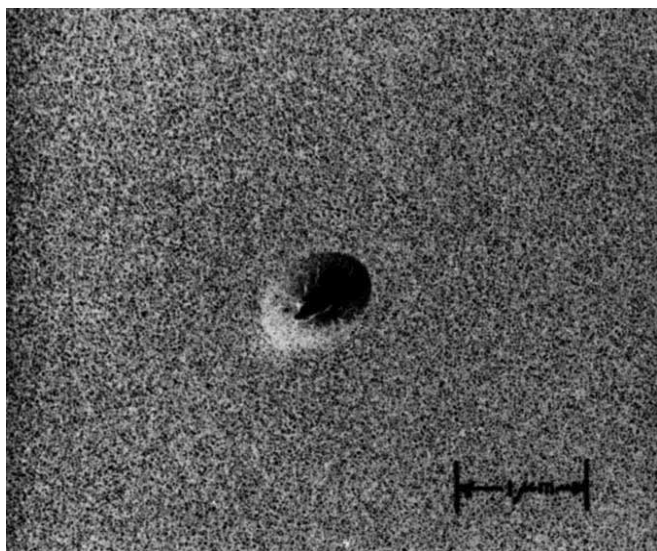


Fig. 1 Two component particle.

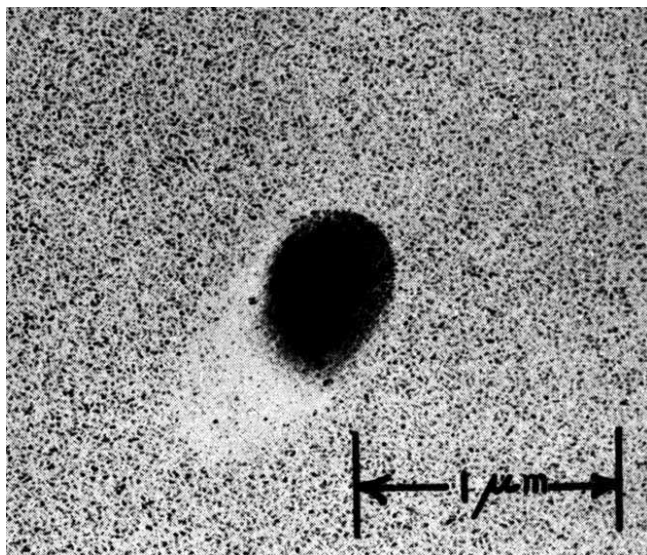


Fig. 2 Two component particle containing multiple inclusions.

Collection Data and Nature of the Particles

We used the Pandora II inflight shadowing technique³ by which the collected particles can be studied as a function of time and altitude intervals. Figs. 1-4 and 6 show examples of the two component particles we have observed: an irregular

Table 1 is a preliminary tabulation of the fluxes of particles collected during a noctilucent cloud display on July 31, 1971, at Kiruna, assuming sedimentation equilibrium, and a particle effective density of 3 gm cm^{-3} (ref. 4). It is important that for a given size range, and within the limitations of particle statistics, the particle influx is approximately constant as a function of height.

Fechtig⁵ found that all the particles detected during a flight two days after our experiment had measurable downward velocities. He suggests that moisture condenses out on the incoming particle nuclei and that noctilucent clouds form because of a change in size of the constituent particles and not because of an increase in their concentration. Two photoelectric polarimeters on our rocket confirmed that the lowest altitude collection interval included a noctilucent cloud layer so the constant flux (Table 1) is consistent with Fechtig's picture. Details of this experiment will be presented at the

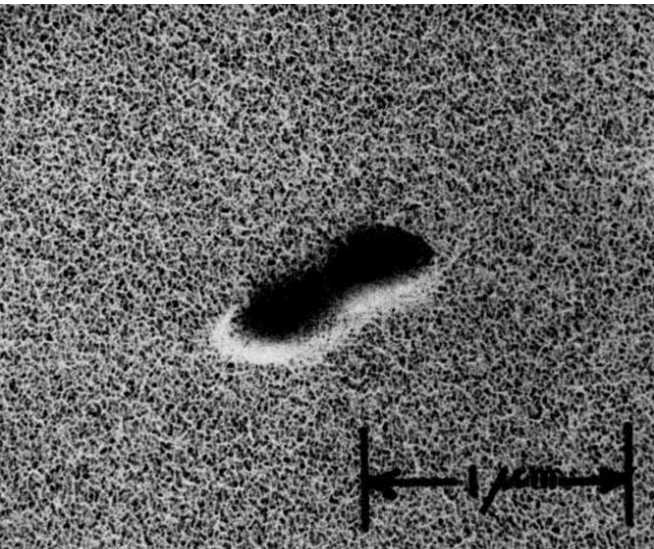


Fig. 3 Two component particle.

COSPAR meeting in 1972; here we point out that the particles enter noctilucent cloud levels from outside the atmosphere.

The rounded, low density material on some of the particles seems to have been associated with the high density material prior to entry into the Earth's atmosphere, and may have been modified by chemical interaction during entry.

The total number densities of submicron particles collected in Sweden (latitude 68° N) are at least an order of magnitude greater than at White Sands (latitude 32° N)³. This datum suggests a cutoff of the size distribution (see Figs. 3 and 6 of ref. 6) indicating that few particles smaller than 0.1 μm average radius are present. No such cutoff was observed during the Pandora P collection at Kiruna (Table 1). For particles with average radius <0.1 μm, the enhancement in Sweden is about 10² times that at White Sands. Because the particles are entering the Earth's atmosphere from outside, the smaller particles seem to be concentrated geomagnetically at high latitude.

We examined the particles with a 'Philips EM 300' electron microscope and analysed them with an AMR mica crystal spectrometer. Table 2 lists the elements possibly present in 8 of the 23 particles examined; most of the particles collected are too small to produce measurable signals. Details of the measurements will be presented later. The results in Table 2 are similar to those obtained in 1970 (refs. 1 and 2).

Particle 15 (Fig. 5) has an average radius 0.08 μm, and seems to contain silicon, tantalum, and rubidium. A particle of this size composed of pure silicon would have an electron optical density comparable to that of the background. The presence

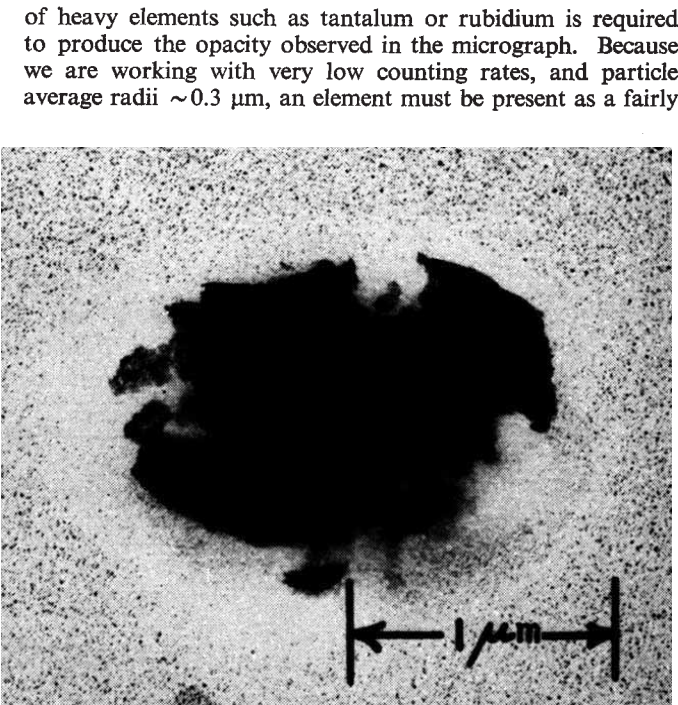


Fig. 4 Large two component particle.

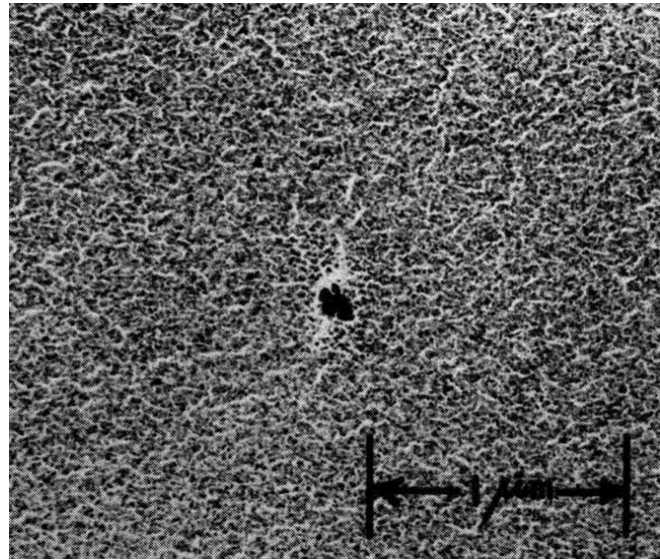


Fig. 5 Single component particle.

Table 1 Pandora P Differential Particle Fluxes

Collection altitude intervals (Km)	Particle radii ranges	<0.05 μm	0.05→0.095 μm	0.1→0.145 μm	>0.15 μm
	Assumed averages	0.038 μm	0.075 μm	0.13 μm	0.2 μm
79-90.4	Number of particles φ (Number m ⁻² s ⁻¹)	6 0.35 × 10 ³	10 1.08 × 10 ³	1 0.19 × 10 ³	3 0.89 × 10 ³
84.5-87.7	Number of particles φ (Number m ⁻² s ⁻¹)	— —	5 0.29 × 10 ³	4 0.36 × 10 ³	3 0.42 × 10 ³
90.8-101.3	Number of particles φ (Number m ⁻² s ⁻¹)	49 1.0 × 10 ³	33 1.6 × 10 ³	4 0.32 × 10 ³	3 0.37 × 10 ³
101.7-113.5	Number of particles φ (Number m ⁻² s ⁻¹)	4 1.3 × 10 ³	9 5.3 × 10 ³	4 3.42 × 10 ³	1 1.3 × 10 ³

Several modes of transport out of the solar atmosphere are possible and a workable model will probably require more than a single mechanism. The initial distribution may be altered by additions of particles formed by condensation cooling from the ambient hot plasma¹².

There is evidence that these particles have been detected in space. Berg and Gerloff¹³ discarded the pulses detected by their micrometeorite experiments on Pioneer 8 and 9 while their sensor was facing the Sun. If we take these solar "disturbance" events to be real, the submicron particle flux from the Sun (free from magnetospheric concentration effects) is approximately 2×10^{-2} particles $\text{m}^{-2} \text{s}^{-1}$ at one AU, and this agrees with the submicron flux observed on lunar spherules¹⁴.

What happens when these solar particles approach the Earth? Because they are probably charged¹⁵, and have low masses, the behaviour will be determined by their velocity. If the particle velocity relative to the Earth exceeds the Earth's orbital velocity, the magnetic rigidity seems too large for simple auroral zone concentration. There may be some high latitude concentration when the Earth's magnetic axis is tilted toward the direction from which the particles arrive. Studies of noctilucent clouds support such a concept of seasonal variation in both the northern and southern hemispheres^{16,17}.

Geophysical and Astrophysical Implications

Continuity of the brightness measurements of zodiacal light with those of the Fraunhofer corona is consistent with a solar origin for the particles; the differing results of various observers of zodiacal light¹⁸ may thus in part be real, and attributable to time and space variations in the solar atmosphere.

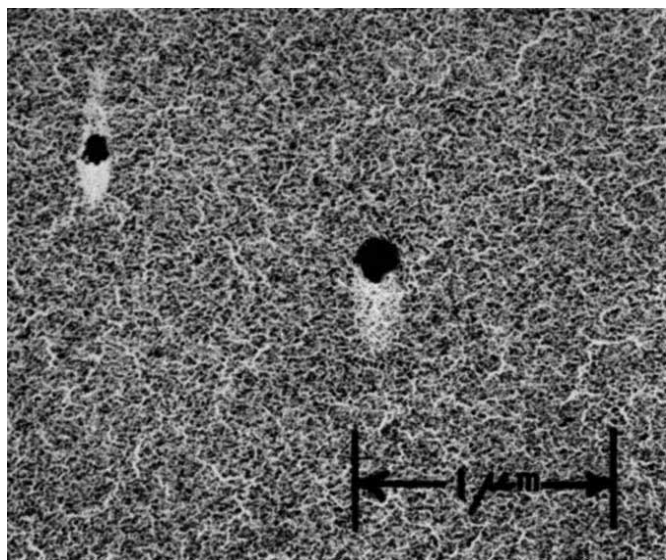


Fig. 7 Single component particle.

The discrepancy between the extension of the meteor flux curves and the rocket collection experiments is understandable: the particles have different origins and the high altitude rocket collections may have the benefit of the cross section of the magnetosphere (including its tail) for flux concentration in the upper atmosphere. The composition discrepancy¹⁹ in the rare earth abundances between lunar (or meteoritic) materials and their estimated abundances in the Sun is, perhaps, understandable. The low apparent abundance of some of

these elements in the Sun may be the result of their being stored in particulate form and so not contributing to the estimates of solar abundance made by spectroscopic methods (J. W. Erkes, personal communication).

These solar particles have a number of geophysical implications. First, they assist greatly in the understanding of noctilucent clouds and suggest that the data on the statistics of noctilucent clouds should be analysed more carefully with regard to solar activity. Second, they seem to contribute to an understanding of the false zodiacal light²⁰ and the zodiacal twilight. Third, the darker background of tropical skies compared with those at higher latitudes may be due to the reduced total scattering from the lower number densities of particles in the magnetosphere at tropical latitudes.

We note that the capture of solar dust by the Earth's upper atmosphere has important meteorological implications. Earlier high altitude rocket flights^{6,7,21,22} suggest that the dust influx is latitude dependent, that there is a minimum level of cleanliness in our atmosphere, and that it is located at low latitudes. It seems likely that solar dust is also an effective nucleating agent for rainfall in the troposphere. Perhaps a missing variable in long range weather forecasting is the upper atmosphere influx of solar dust.

The dust we observe at the Earth must also impinge on other planets in the solar system. Mariner 9 observations²³ have shown the presence of a noctilucent cloud-like layer in the upper Martian atmosphere.

If the Sun is emitting submicron particles it is likely that many others stars do. This has ramifications for the study of the interplanetary medium, the interstellar medium, and stellar astrophysics generally. For example, particle formation in stars may be expected to play a role in the interpretation of nebulosities in their vicinity, to help explain the anomalous rare earth abundances in peculiar A stars, and to contribute to the understanding of the high atomic weight component in cosmic ray spectra. The role of chemical differentiation in particle formation and transport from stars will have to be carefully studied.

We thank M. Dubin for many helpful discussions, and acknowledge the technical assistance of the Dudley Observatory staff, the Goddard Sounding Rocket Division, and Wallops Island personnel. This programme was supported by NASA and the USAF.

Received February 11; revised June 9, 1972.

¹ Hallgren, D. S., Hemenway, C. L., Mohnen, V. A., and Tackett, C. D., *Space Research*, **12** (Akademie-Verlag, Berlin, in the press).

² Hemenway, C. L., and Hallgren, D. S., in *International Astronomical Union Colloquium No. 13*, Albany, 1971 (in the press).

³ Hallgren, D. S., and Hemenway, C. L., *Space Research*, **11**, 377 (Akademie-Verlag, Berlin, 1971).

⁴ Soberman, R. K., and Hemenway, C. L., *J. Geophys. Res.*, **70**, 4943 (1965).

⁵ Fechtig, H., *Space Research*, **12** (Akademie-Verlag, Berlin, in the press).

⁶ Hemenway, C. L., and Hallgren, D. S., in *Space Research*, **10**, 272 (North-Holland, Amsterdam, 1970).

⁷ Hemenway, C. L., and Hallgren, D. S., *Space Research*, **9**, 140 (North-Holland, Amsterdam, 1969).

⁸ Hemenway, C. L., Hallgren, D. S., Laudate, A. T., Patashnick, H., Renzema, T. S., and Griffith, O. K., *Space Research*, **11**, 393 (Akademie-Verlag, Berlin, 1971).

⁹ Griffith, O. K., Renzema, T. S., Hallgren, D. S., and Hemenway, C. L., *Space Research*, **11**, 383 (Akademie-Verlag, Berlin, 1971).

¹⁰ Greenberg, J. M., in *Space Research*, **9**, 111 (North-Holland, Amsterdam, 1969).

¹¹ Bray, R. J., and Loughhead, R. E., *Sunspots*, 65 (Wiley and Sons, New York, 1965).

¹² Zel'dovich, Ya. B., and Raizer, Yu. P., *Physics of Shock Waves and High Temperature Hydrodynamic Phenomena* (Academic, New York, 1967).

- ¹³ Berg, O. E., and Gerloff, U., in *Space Research*, **11**, 225 (Akademie-Verlag, Berlin, 1971).
- ¹⁴ Fechtig, H., in *International Astronomical Union Colloquium No. 13*, Albany, 1971 (in the press).
- ¹⁵ Rhee, J. W., *University of Maryland Technical Report No. 596* (1956).
- ¹⁶ Volz, F., in *Noctilucent Clouds International Symposium*, Tallin, 1966, 61 (Izdatel'stvo VINITI, Moscow, 1967).
- ¹⁷ Fogle, B., in *Noctilucent Clouds International Symposium*, Tallin, 1966, 29 (Izdatel'stvo VINITI, Moscow, 1967).
- ¹⁸ Weinberg, J. L., in *Space Research*, **10**, 233 (North-Holland, Amsterdam, 1970).
- ¹⁹ Morrison, G. H., et al., *Proc. of the Apollo 11 Lunar Science Conference*, Houston 1970, 1383 (Pergamon, New York, 1970).
- ²⁰ Divari, N. B., *Astron. Zh.*, **26**, 355 (1949).
- ²¹ Hemenway, C. L., and Soberman, R. K., *Astron. J.*, **67**, 256 (1962).
- ²² Hemenway, C. L., Soberman, R. K., and Witt, G., *Tellus*, **16**, 84 (1964).
- ²³ Masursky, H., et al., *Science*, **175**, 294 (1972).

Moon Model—An Offset Core

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A lunar model having an asymmetric core explains the offset centre of gravity, moment of inertia, mascons and maria. A possible evolution theory is also presented.

A MODEL of the Moon in which the core is offset helps to account for the offset of the centre of gravity from the centre of the optical figure, the moments of inertia of the Moon, the "mascons", the localization of the maria basins on the near side of the Moon, the igneous nature of rocks and the remanent magnetism.

Our model for the Moon is shown in Fig. 1. The moments of inertia for this model are

$$\begin{aligned}
 I_z &= \frac{2}{5} V_0 \rho_0 r_0^2 \left[1 + \frac{\rho_1}{\rho_0} \left(\frac{r_1}{r_0} \right)^5 - \left(\frac{r_1}{r_0} \right)^5 \right] \\
 &+ V_0 \rho_0 \left[c^2 + g^2 + (d^2 + h^2) \left(\frac{r_1}{r_0} \right)^3 \frac{\Delta \rho}{\rho_0} \right] \\
 I_x &= \frac{2}{5} V_0 \rho_0 r_0^2 \left[1 + \frac{\rho_1}{\rho_0} \left(\frac{r_1}{r_0} \right)^5 - \left(\frac{r_1}{r_0} \right)^5 \right] \\
 &+ V_0 \rho_0 \left[e^2 + g^2 + (h^2 + f^2) \left(\frac{r_1}{r_0} \right)^3 \frac{\Delta \rho}{\rho_0} \right] \\
 I_y &= \frac{2}{5} V_0 \rho_0 r_0^2 \left[1 + \frac{\rho_1}{\rho_0} \left(\frac{r_1}{r_0} \right)^5 - \left(\frac{r_1}{r_0} \right)^5 \right] \\
 &+ V_0 \rho_0 \left[e^2 + c^2 + (d^2 + f^2) \left(\frac{r_1}{r_0} \right)^3 \frac{\Delta \rho}{\rho_0} \right]
 \end{aligned}$$

where V =volume, ρ =density, r =radius of sphere, $\Delta\rho = \rho_1 - \rho_0$, c =centre of gravity offset in x-direction, e =centre of gravity offset in y-direction, g =centre of gravity offset in z-direction, d =distance from centre of gravity to centre of volume V_1 in x-direction, f =distance from centre of gravity to centre of volume V_1 in y-direction, and h =distance from centre of gravity to centre of volume V_1 in z-direction.

Since the spherical harmonic coefficients J_2 and C_{22} in the lunar potential relate the moments of inertia, one can write

$$J_2 = \frac{1}{Mr_0^2} \left[I_z - \frac{1}{2} I_x - \frac{1}{2} I_y \right] = \frac{1}{2r_0^2 k} (c^2 + g^2 - 2e^2)$$

$$C_{22} = \frac{1}{4Mr_0^2} [I_y - I_x] = \frac{1}{4r_0^2 k} (c^2 - g^2)$$

where

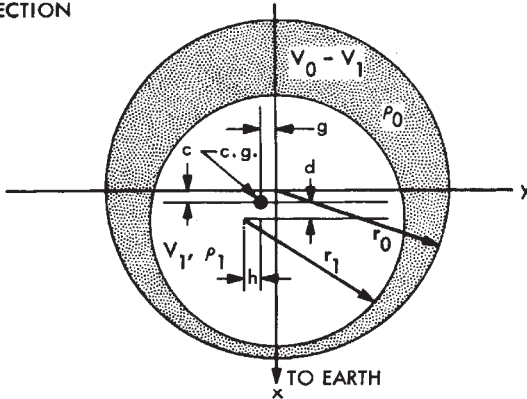
$$k = \frac{\rho_{av}}{\rho_0} - 1 = \frac{\Delta \rho}{\rho} \left(\frac{r_1}{r_0} \right)^3$$

and $d=c/k$, $f=e/k$, $h=g/k$, and M =mass. Using the values of $J_2 = 0.205 \times 10^{-3}$, $C_{22} = 0.22 \times 10^{-4}$, $c = 2.5 \text{ km}^{8,10-16}$, $e = 1.0 \text{ km}^{19}$, and $\rho_{av} = 3.3 \text{ g cm}^{-3}$, the density differential necessary to account for these terms as a function of r_1 (the core size) can be computed. These data are plotted in Fig. 2. The values above produce a unique value for k of 0.0073, which in turn determines an outer crust density, ρ_0 , of 3.315 g cm^{-3} and a centre of the core 466 km from the centre of mass. Therefore, if a density differential ($\Delta\rho$) of 0.4 g cm^{-3} is assumed, a core 700 km in diameter is obtained. This implies an outer shell with a 572-km thickness toward the Earth and a 1,504-km thickness on the far side. Modest changes in density near the centre of the Moon are sufficient to account for the observed J_2 and C_{22} , the classic moment of inertia terms.

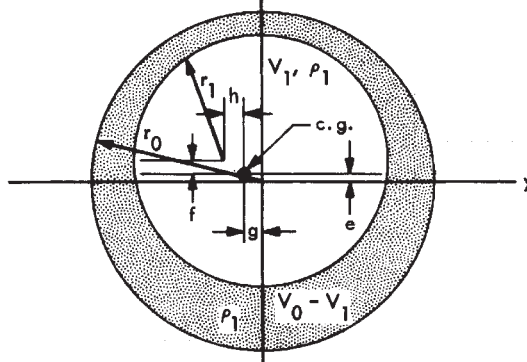
Possible Evolution

In the proposed model the Moon has a core whose centre is offset from the centre of the outside spheroid towards the Earth. Such a core will be formed if the Moon were entirely

POLAR PROJECTION



EQUATORIAL PROJECTION (x AXIS)



EQUATORIAL PROJECTION (y AXIS)

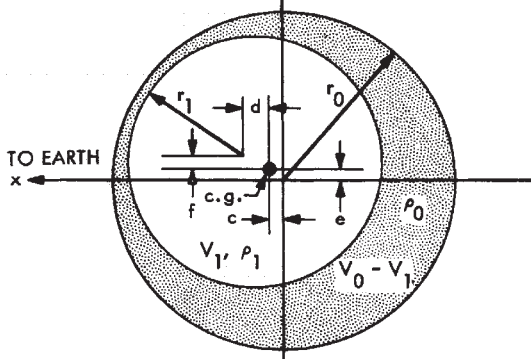


Fig. 1 Three views of geometry of offset core.

molten at some time in its past, and on solidification was synchronous with the Earth. A molten lunar surface is shown by igneous lunar samples brought back by the Apollo missions^{4-6,9}. The Apollo seismometer experiments (G. Latham, private communication) and the electrical conductivity data²² from both the Explorer 35 and the Apollo surface magnetometers indicate a "layered" lunar crust which would result if the Moon were totally or mainly molten at some time in the past.

The molten Moon would cool mainly by radiation into space, while its Earth-facing surface would be heated by the Earth. The Sun's heat would also heat the outer layers but this heat would be lost during the lunar night. Thus the Sun's heat would not affect the lunar cooling rates. The same argument

can be applied to the reflexion of the Sun's rays by the Earth, where the main source of heat is the Earth's primordial heat. Assuming that the Earth and Moon act like black bodies, the solidification rate of the Moon is proportional to the amount of heat lost, and the effects of the Sun's and Earth's reflexion of sunlight are zero, the cooling rate of a unit area perpendicular to the line joining the centre of the Moon and the centre of the Earth, on the lunar near side, is

$$\Delta q_r = - \sigma \left(T_M^4 - \frac{R_E^2}{R_{EM}^2} T_E^4 \right)$$

where σ = the Stefan-Boltzmann constant, T_M = temperature of the Moon, T_E = temperature of the Earth, R_E = radius of the Earth, R_{EM} = distance between the Earth and Moon.

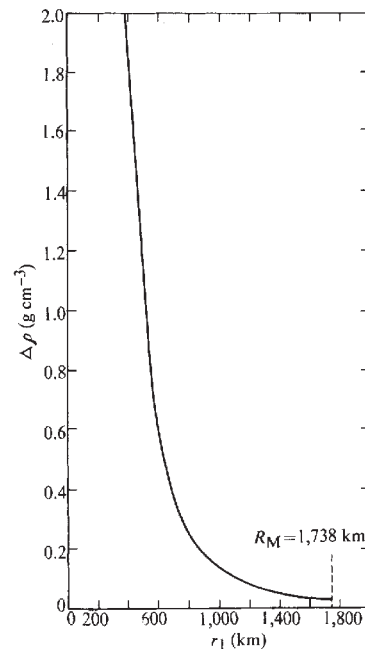


Fig. 2 Values of $\Delta \rho$ against r_1 for offset core model.

For the lunar far side,

$$\Delta q_b = - \sigma T_M^4$$

(The sign convention is that negative heat is radiated and positive heat is absorbed.)

The ratio of these is

$$\frac{\Delta q_r}{\Delta q_b} = \frac{T_M^4 - \frac{R_E^2}{R_{EM}^2} T_E^4}{T_M^4}$$

If this ratio is to remain constant it must represent the ratio of crust build-up on the near side to the rate of crust build-up on the far side.

Fig. 3 is a plot of $\Delta q_r/\Delta q_b$ as a function of T_E for five different primordial Moon temperatures, assuming its present orbit. For reasonable Moon temperatures (1,200–2,000 K) and primordial Earth temperatures of $> 6,000$ K, significant differences in crust build-up will occur. If the Moon were closer to the Earth and were still synchronous, lower Earth temperatures

would be required to cause this crust build-up difference. The dashed curve on Fig. 3 is a plot of the $\Delta q_t/\Delta q_b$ against Earth temperatures for a Moon temperature of 1,200 K and an Earth-Moon distance half its present value.

We explain the mascons² on the near side in the following way. If the Moon is bombarded by a random selection of sizes and velocities of meteorites from all directions, those hitting the near side are likely to weaken the thinner crust on the near side more than on the far side. When volcanic magma flows under pressure²¹, these flows would be more likely on the thinner side than on the far side. The mascons represent dense lavas filling the old crater basins⁹.

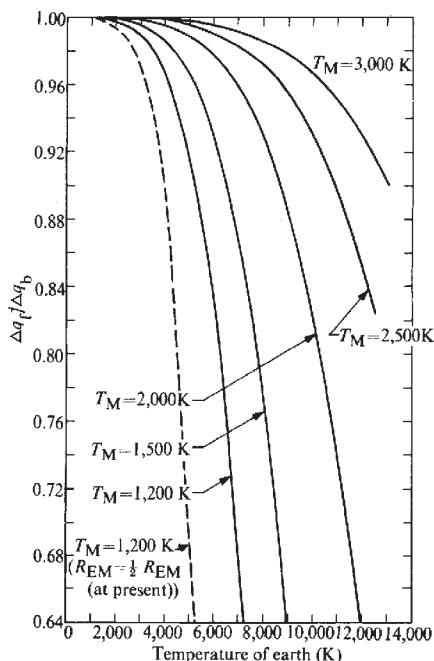


Fig. 3 Values of $\Delta q_t/\Delta q_b$ against temperature of the Earth.

Could the molten Moon be in captured rotation with the Earth? Captured rotation concerns the inequality between the A and B moments of inertia of the Moon, the moments of inertia with respect to the x and y axes, respectively. Bodies in rotation about a larger body tend to assume the positions of least inertia with respect to the central body²⁰. If the orbit of the satellite body is nearly equatorial to the central body and if the moments of inertia in this plane are unequal, the body will assume an orientation such that one side always faces the central body. The concept of the moments of inertia being permanently unequal is untrue of the fluid sphere necessary in this model.

We have considered the equilibrium shape of a fluid body acted on by its own gravity rotation and outside pull. There will be a small distortion in the Earth-Moon system in the direction of this pull. So long as the body remained fluid, this distortion would maintain its alignment in the pull direction, and when the surface solidified, this distortion would be "frozen" in. As the body rotated, the pull on this distortion would tend to slow its rotation, and if the rotation rate were initially slow or if the pull were great enough, the body would cease its total rotation with respect to the central body and would oscillate, or librate, keeping one face roughly facing the central body. The mechanism described in the model would then tend to slow the body's rotation rate further until it had become completely "captured". This mechanism seems particularly likely if the Moon accreted cold and was then melted by its radio-

activity. The rotation rate would probably be near the "capture" rate when it melted.

The newly formed crust would have low heat conductivity and therefore the cooling rate would diminish quickly when the crust was formed. However, the thermal properties of materials near their melting points differ from those at lower temperatures, and the heat transfer properties of the cooling crust might not be as low as expected.

It is obvious that the assumption that the ratio of $\Delta q_t/\Delta q_b$ remains constant in time is unrealistic, and was introduced only to allow an argument such as the one above to be made. Assuming the orbit of the Moon around the Earth to be nearly circular, the constant ratio assumption is expressible as:

$$\frac{\partial T_M}{\partial t} = \frac{T_M}{T_E} \frac{\partial T_E}{\partial t}$$

The model is linearized in time, and can be treated as a first order approximation to the true system.

Further evidence for a molten core comes also from the Apollo rocks. The remanent magnetization in the Apollo 11 rocks indicates that at the time of their formation the magnetic field in the area of the Apollo 11 site was significantly higher than at present⁴. These data could be interpreted in terms of a shrinking central core of molten material.

Received April 4, 1972.

- ¹ Kopal, Zdenek, *An Introduction to the Study of the Moon* (D. Reidel Publishing Company, Dordrecht, Holland, 1966).
- ² Muller, P. M., and Sjogren, W. L., *Science*, **161**, 680 (1968).
- ³ Michael, W. A., *Fourteenth General Assembly of the International Union of Geodesy and Geophysics Meeting*, Lucerne, Switzerland (1967).
- ⁴ Lunar Sample Analysis Planning Team, *Science*, **167**, 449 (1970).
- ⁵ Lunar Sample Preliminary Examination Team, *Science*, **167**, 1325 (1970).
- ⁶ *Apollo 14 Preliminary Science Report*, NASA SP-272, National Aeronautics and Space Administration, Washington, DC (1971).
- ⁷ Ransford, G. A., Wollenhaupt, W. R., and Gizzell, R. M., *NASA-TN-D-6082* (National Aeronautics and Space Administration, Washington, DC, 1970).
- ⁸ Wollenhaupt, W. R., and Ransford, G. A., *Bull. Amer. Astron. Soc.*, **3**, Part II (1971).
- ⁹ Apollo 15, *Preliminary Science Report* (in the press).
- ¹⁰ Muller, P. M., and Sjogren, W. L., in *Proceedings of the International Astronomical Union Symposium No. 47, The Moon* (University of Newcastle upon Tyne, England, in the press).
- ¹¹ Sjogren, W. L., *Measure of the Moon* (edit. by Kopal, Z., and Goudas, C.), 341 (D. Reidel Publishing Company, 1967).
- ¹² Shapiro, A., Uliana, E. A., Yaplee, B. S., and Knowles, S. H., *Moon and Planets II* (North-Holland Publishing Company, 1968).
- ¹³ Wells, William D., *AAS Paper 71-337* (AAS/AIAA Astrodynamics Specialists Conference, Ft. Lauderdale, Florida, 1971).
- ¹⁴ US Army Topocommand, Lunar 1 : 100,000 Topomaps II P-2 (December 1967); II P-6 (December 1967); III P-II (January 1968); II P-13 (December 1967); Lunar 1 : 250,000 Topographic Photomaps V-23; 1-Rima Hyginus, second ed. (October 1970); V-24-Hipparchus (November 1970).
- ¹⁵ US Air Force Aeronautical Chart and Information Center (ACIC) Lunar 1 : 100,000 Topomaps II P-8 (December 1967); III P-12 (March 1968); III P-9 (March 1968); Lunar 1 : 250,000 Topographic Photomaps; III-5-18-Mosing C (December 1969); III-5-23-Fra Mauro, second ed. (October 1970).
- ¹⁶ Garthwaite, K., Holdridge, D. B., and Mulholland, J. D., *Astron. J.*, **75**, 1133 (1970).
- ¹⁷ Lorell, J., *The Moon*, **1**, 190 (1970).
- ¹⁸ Lorell, J., *Supporting Research and Advanced Development, Space Programs Summary 37-45*, 4 (Jet Propulsion Laboratory, Pasadena, California, 13, 1967).
- ¹⁹ O'Keefe, J. A., and Cameron, W. S., *Icarus*, **1**, 271 (1962).
- ²⁰ Jeffreys, H., *The Earth* (Cambridge University Press, 1962).
- ²¹ Wise, D. V., and Yates, M. T., *J. Geophys. Res.*, **75**, 261 (1970).
- ²² Sonnet, C. R., Colburn, D. S., Dyal, P., Parkin, C. W., Smith, B. F., Schubert, G., and Schwartz, K., *Nature*, **230**, 359 (1971).
- ²³ Sjogren, W. L., *J. Geophys. Res.*, **76**, 7021 (1971).

LETTERS TO NATURE

PHYSICAL SCIENCES

Infrared Photometry of Markarian 231

SEVERAL lists of galaxies with ultraviolet continua have been published by Markarian¹⁻³ and Markarian and Lipovetsky⁴. Approximately 10% of these objects are spectroscopically similar to Seyfert galaxies. Sargent⁵ has pointed out that Markarian's method of searching with an objective prism tends to select those Seyfert galaxies where the nuclei, with their characteristic blue colours, contribute most of the light. Thus, the Seyfert galaxies on Markarian's lists tend to have more luminous nuclei than the classical Seyferts.

Markarian 231 is such a Seyfert galaxy with a very luminous nucleus. Arakelian *et al.*⁶ find an emission redshift of $z=0.041$. Using a Hubble constant of $50 \text{ km s}^{-1} \text{ Mpc}^{-1}$ and the photographic magnitude 14.1 given by Zwicky and Herzog⁷, we find an intrinsic photographic magnitude $M_p = -22.9$. (The value $M_p = -19.8$ given by Sargent⁵ is apparently based on a typographical error in Markarian's paper³ pointed out by Adams and Weedman⁸.) The nuclei of classical Seyfert galaxies have values of M_p of the order of -18 . The high luminosity of Markarian 231 is more like that of quasistellar objects, and multiple absorption lines displaced from the emission lines⁸ are common in quasistellar spectra.

calibration of the photometry may be uncertain by an additional 20%. Two other measurements are included in the figure, the photographic magnitude⁸ and the radio emission^{9,10}. No radio source is found at the position of Markarian 231. The upper limit of 0.1 flux unit at 1,415 MHz is derived from the Ohio V radio survey¹⁰.

Because the flux is rising toward longer infrared wavelengths, where the object has not been observed, we cannot determine the luminosity precisely. A conservative estimate can be based on the observed flux in the 8–14 μ band. The total luminosity may be proportional to this flux¹¹. The flux between 8–14 μ is $1.8 \times 10^{-13} \text{ W m}^{-2}$; this gives a power of $1.2 \times 10^{45} \text{ erg s}^{-1}$ based on the redshift $z=0.041$ and a Hubble constant of $50 \text{ km s}^{-1} \text{ Mpc}^{-1}$. This power is a factor of 1.3×10^6 greater than the Galaxy, a factor of 18 greater than NGC 1068, and only a factor of 35 smaller than 3C 273 in this band. Indeed, the 8–14 μ power of Markarian 231 is greater than the total luminosity of the galactic centre by a factor of 3.8×10^3 (see ref. 11). Thus Markarian 231 is the most luminous galaxy yet observed. These observations provide additional support for the hypothesis that similar physical processes are taking place in the nuclei of galaxies and in quasistellar objects.

We thank T. Adams for discussions. This research was supported by the National Science Foundation.

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Received June 9, 1972.

- ¹ Markarian, B. E., *Astrofizika*, **3**, 55 (1967).
- ² Markarian, B. E., *Astrofizika*, **5**, 443 (1969).
- ³ Markarian, B. E., *Astrofizika*, **5**, 581 (1969).
- ⁴ Markarian, B. E., and Lipovetsky, V. A., *Astrofizika*, **7**, 511 (1971).
- ⁵ Sargent, W. L. W., *Astrophys. J.*, **173**, 7 (1972).
- ⁶ Arakelian, M. A., Dibai, E. A., Esipov, V. F., and Markarian, B. E., *Astrofizika*, **7**, 177 (1971).
- ⁷ Zwicky, F., and Herzog, E., *Catalogue of Galaxies and Cluster of Galaxies*, **4** (California Institute of Technology, 1968).
- ⁸ Adams, T. F., and Weedman, D. W., *Astrophys. J. Lett.*, **173**, L109 (1972).
- ⁹ Dixon, R. S., *Astrophys. J. Supp.*, **20**, 1 (1970).
- ¹⁰ Brundage, R. K., Dixon, R. S., Ehman, J. R., and Kraus, J. D., *Astron. J.*, **76**, 777 (1971).
- ¹¹ Kleinmann, D. E., and Low, F. J., *Astrophys. J. Lett.*, **159**, L165 (1970).

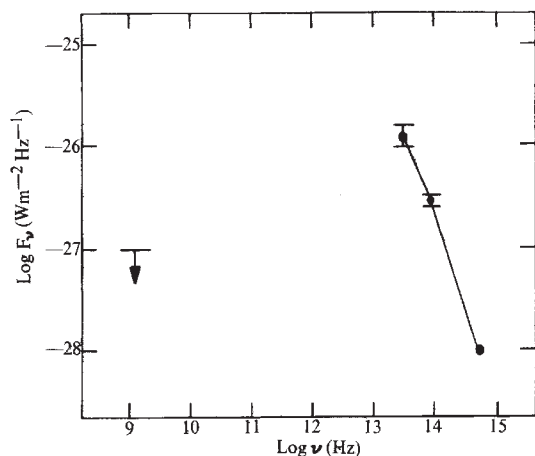


Fig. 1 Spectrum of Markarian 231. References to the measurements are given in the text.

We have observed Markarian 231 in the infrared to gain a better understanding of the energy emitted by this object. Observations were made with a liquid helium cooled, gallium-doped germanium bolometer at the 60-inch Tillinghast reflector of the Smithsonian Astrophysical Observatory. The photometry employed filters with effective wavelengths of 3.5 and 10.8 μ and with passbands of $\Delta\lambda = 1 \mu$ and 6μ respectively. The object was observed on May 14 and 15, 1972. Flux from both the disk (12 arc s diameter) and the star-like nucleus entered the 9 arc s aperture.

The results are shown in Fig. 1. The uncertainty is the standard deviation of the mean of the integrations, and the

Plate Motions relative to the Deep Mantle and the Development of Subduction Zones

THE development of subduction zones may depend on the motion of the two converging lithospheric plates relative to the underlying deep mantle. It is likely that the plates move much more rapidly than the underlying mantle¹⁻⁴, the return flow being diffused through a large region^{1,5}. The deep mantle is thus nearly stationary and the horizontal motion of

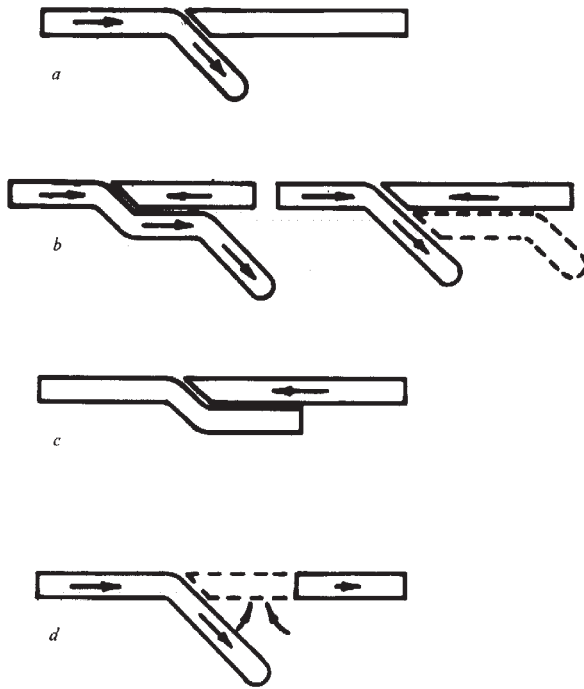


Fig. 1 The development of subduction zones. (a) The down-side plate sinks as an inclined slab, the arc-side plate is stationary; (b) the down-side plate sinks, the arc-side plate overrides the inclined slab and the overridden inclined slab may eventually be cut off; (c) the down-side plate is stationary and is overridden by the arc-side plate; (d) the down-side plate sinks and the arc-side plate retreats leaving a gap that is filled by upwelling.

sinking plates that extend to depths of 700 km must be significantly restrained.

The absolute motion of the converging plates (with respect to the deep mantle) can be estimated from two surface manifestations of the deep mantle; volcanism over hot spots or mantle plumes^{1,6,7}, and the positions of sinking plates behind subduction zones revealed Benioff earthquake zones and andesitic volcanism.

When a dipping plate behind a trench penetrates stationary mantle so that its horizontal position is nearly fixed, subduction zones develop according to the absolute motion of the two converging plates (Fig. 1).

(a) When the arc-side (non-sinking) plate is stationary, the down-side (sinking) plate moves toward the subduction zone and sinks as an inclined slab (Fig. 1a) to give the "normal" subduction zone, which is stable. Sinking continues as long as the plates converge and continental crust is not encountered on the down-side plate.

(b) When the arc-side and down-side plates both move toward the subduction zone (Fig. 1b), the arc-side plate overrides the sinking, inclined slab until the friction along the horizontal surface between the two plates causes a new zone of sinking and the inclined slab is cut off. Western North America and the Caribbean arcs have developed in this way.

(c) When the arc-side plate moves toward the subduction zone and the down-side plate is stationary or moving away at a slower rate (Fig. 1c), the arc-side plate overrides the down-side plate. When the friction between the plates becomes large, convergence stops and the plates become coupled. Unless the arc-side plate is continental, the plates flip over, the former arc-side plate sinking as an inclined slab.

(d) When the arc-side plate moves away from the subduction zone while the down-side plate is moving toward it and sinking in an inclined zone (Fig. 1d), a gap forms between the subduction zone and the arc-side plate that must be filled by upwelling from below. In the western Pacific trenches and arcs the inland seas have formed in the widening gap between the subduction zones and the receding Asia, Mariana and Australia plates.

These major differences in the development of subduction zones are accompanied by significant differences in the dip angle of the upper parts of the sinking plates. The sinking angle is shallow, for the upper part of a sinking slab is overridden by the arc-side plate whereas the sinking angle is steep when the upper part of the sinking slab is being pulled by a receding arc-side plate, a pattern consistent with the earthquake pattern of many sinking zones⁸.

It has been suggested⁹ that the North American plate has overridden the subduction zone at its western margin. The empirical relation between the ratio of K_2O to SiO_2 in andesitic volcanics and the depth to the Benioff seismic zone in active subduction zones¹⁰ is used to estimate the position of extinct or palaeoseismic zones (Fig. 2). In the western United States there is a pattern from the Late Cretaceous to the Miocene, of volcanism shifting slowly from the western to eastern Cordillera and then jumping back to the west, to the site of the present or recently active sinking zone. Palaeoseismic zones for both before and after the jump indicate a slow overriding of the sinking plate by the continent at 1–2 cm per year since the Late Mesozoic. The rapid opening of the Atlantic Ocean started at about that time, initiating the westward motion of North America. This rate is similar to the present rate of absolute motion of the North American plate¹.

The existence of two old sinking zones under the Cordillera is substantiated by the low heat flow existing on the immediate arc-side of active trenches^{11,12} because of the downward movement of the cool dense plate. Such a low will persist for several tens of millions of years after sinking stops because

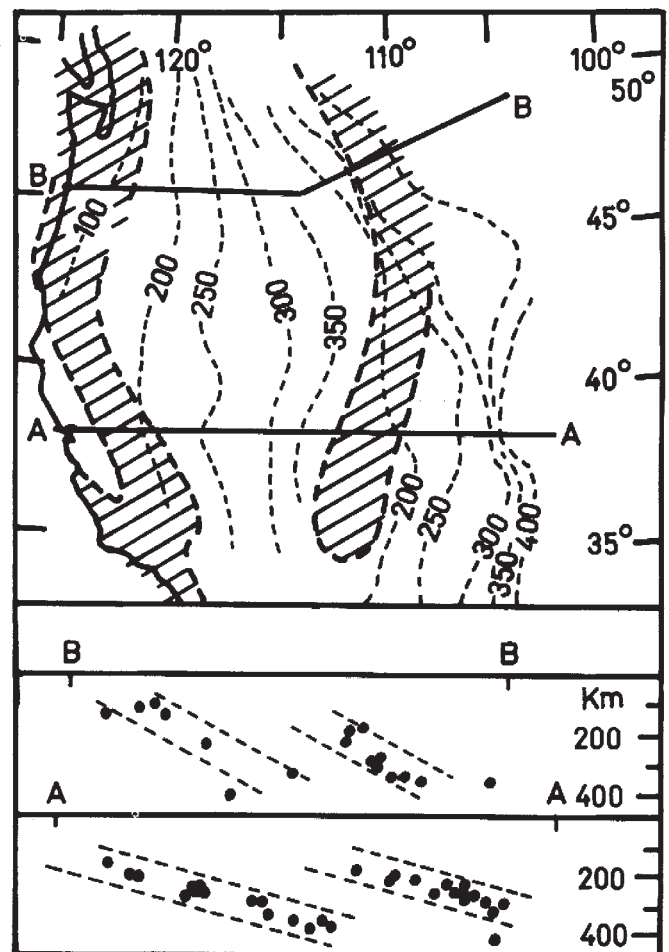


Fig. 2 The palaeoseismic Benioff zones⁹ (A) and zones of low heat flow^{13,14} (B). The contours show depths in km to the palaeoseismic zones and the hatched areas have heat flows of less than $1.5 \mu\text{cal}/\text{cm}^2$ (corrected for variations in near surface radioactive heat production).

of the long thermal time constant of plates. Pronounced low heat flow zones are located almost exactly over the shallow parts of the palaeoseismic zones¹³⁻¹⁵ (Fig. 2). Studies of geomagnetic induction have shown two zones of low upper mantle temperature with shallow, high mantle electrical conductivity in the region of the postulated overridden plate^{16,17}. There are high heat flows, low seismic Pn velocities and a shallow, low velocity layer in this region^{18,19} which may be caused by high radioactive heat production of the overridden plate²⁰.

Movement of the arc-side plate away from a subduction zone requires an upwelling to fill the widening gap. Extension within the marginal basins behind the arcs of the western Pacific Ocean²¹⁻²³ may be formed in this way. Behind the Mariana arc the average rate of extension has been about 4 cm per year since the Eocene^{23,24}, a rate equal to the estimated rate of absolute eastward motion of the Mariana plate¹. The opening rate of the interarc basin behind the Tonga-Kermadec arcs of 1 cm per year^{25,26} is similar to the estimated component of velocity of the Australian plate perpendicular to the arc¹. Karig²³ suggests that all the west Pacific arcs may have formed at the continental margins and migrated eastward. An extension of about 2.5 cm per year is required to maintain the observed high heat flow¹² in the Sea of Japan.

These examples substantiate that motion in the upper 600 km of the mantle beneath the lithosphere is slow compared with that of plate motions. The development of subduction zones depends on the absolute plate movements.

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- ¹ Morgan, W. J., *Nature*, **230**, 42 (1971).
- ² Jacoby, W. R., *J. Geophys. Res.*, **75**, 5671 (1970).
- ³ Hales, A. L., *Earth Planet. Sci. Lett.*, **6**, 31 (1969).
- ⁴ Ringwood, A. E., in *Geophys. Monogr.*, **13**, 1 (1969).
- ⁵ Schubert, G., and Turcotte, D. L., *J. Geophys. Res.*, **77**, 945 (1972).
- ⁶ Wilson, J. T., *Phil. Trans. Roy. Soc., A*, **258**, 145 (1965).
- ⁷ Dietz, R. S., and Holden, J. C., *J. Geophys. Res.*, **75**, 4939 (1970).
- ⁸ Isacks, B., and Molnar, P., *Rev. Geophys.*, **9**, 103 (1971).
- ⁹ Lipman, P. W., Prostka, H. J., and Christiansen, R. L., *Science*, **174**, 821 (1971).
- ¹⁰ Dickinson, W. R., *Rev. Geophys.*, **8**, 813 (1970).
- ¹¹ Lee, W. H. K., and Uyeda, S., in *Geophys. Monogr.*, **8**, 87 (1965).
- ¹² McKenzie, D. P., and Sclater, J. G., *J. Geophys. Res.*, **73**, 3173 (1968).
- ¹³ Roy, R. F., Blackwell, D. D., and Decker, E. R., in *Nature of the Solid Earth* (edit. by Robertson, E.) (McGraw-Hill, New York, 1972).
- ¹⁴ Blackwell, D. D., in *Geophys. Monogr.*, **14**, 169 (1971).
- ¹⁵ Blackwell, D. D., *Trans. Amer. Geophys. Un., EOS*, **11**, 924 (abst., 1971).
- ¹⁶ Porath, H., Gough, D. I., and Camfield, P. A., *Geophys. J.*, **23**, 387 (1971).
- ¹⁷ Schmucker, U., *Bull. Scripps Inst. Oceanogr. Tech. Ser.*, **14** (1970).
- ¹⁸ Herrin, E., *Geophys. Monogr.*, **13**, 243 (1969).
- ¹⁹ Archambeau, C. B., Flinn, E. A., and Lambert, D. G., *J. Geophys. Res.*, **74**, 5825 (1969).
- ²⁰ Aumento, F., and Hyndman, R. D., *Earth Planet. Sci. Lett.*, **12**, 373 (1972).
- ²¹ Dietz, R. S., *Bull. Geol. Soc. Amer.*, **65**, 1199 (1954).
- ²² Carey, S. W., in *Continental Drift, a Symposium* (edit. by Carey, S. W.), 177 (Univ. of Tasmania Press, Hobart, 1958).
- ²³ Karig, D. E., *Geol. Soc. Amer. Bull.*, **82**, 323 (1971).
- ²⁴ Karig, D. E., and Glassley, W. E., *Bull. Geol. Soc. Amer.*, **81**, 2143 (1970).
- ²⁵ Karig, D. E., *J. Geophys. Res.*, **75**, 239 (1970).
- ²⁶ Sclater, J. G., Hawkins, J. W., Mammereickx, and Chase, C. G., *Bull. Geol. Soc. Amer.*, **83**, 505 (1972).
- ²⁷ Oxburgh, E. R., and Turcotte, D. L., *J. Geophys. Res.*, **76**, 1315 (1971).

The Somerset Saltfield

IN 1910 a borehole¹ was sunk near Puriton, a village in Somerset, 3 miles (4.8 km) north-north-east of Bridgwater. This borehole, which was an unsuccessful attempt to find coal, fortuitously discovered rock salt within the Keuper Marl between the depths of about 183 m and 219.5 m from the surface. Subsequently the salt deposits were worked, over a period of eleven years, by means of brine-pumping². Although rock salt is relatively abundant in the Keuper Marl of the United Kingdom, the Puriton Borehole was the first discovery of the mineral, in economic quantities, in the south of England.

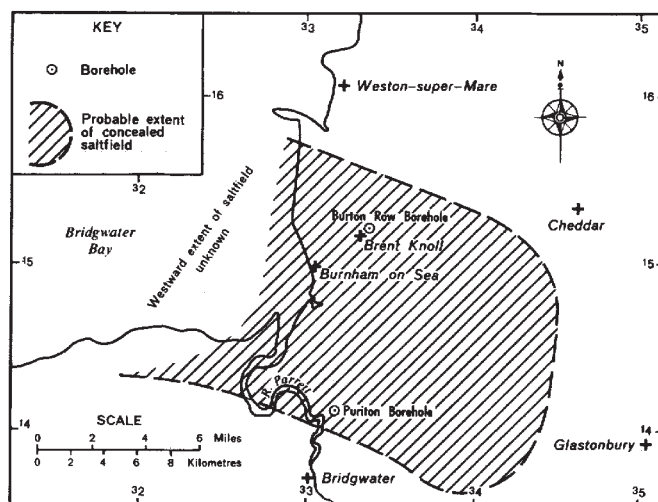


Fig. 1 Probable area of concealed rock salt in Somerset.

A recent borehole made for the Institute of Geological Sciences near Brent Knoll, Somerset, has shown the salt-bearing strata to extend northwards at a similar stratigraphical level in the Keuper Marl. This borehole, known as the Burton Row Borehole, is situated 1,325 m due north of St Michael's Church, Brent Knoll (National Grid Reference ST 3356 5208). It was drilled to investigate the detailed Lias and Triassic stratigraphy in the Central Somerset Basin, in which the solid geology is mantled by alluvial deposits of the Somerset Levels. Brent Knoll itself is an isolated inlier of Middle and Upper Lias strata surrounded by alluvial deposits; it is the only place in this part of the Somerset Levels where the higher parts of the Lower Lias are known, with certainty, to occur.

The succession proved in the Burton Row Borehole is as follows: Hillwash and alluvium to 8.40 m, Lias (including White Lias) to 410.78 m, Rhaetic to 422.06 m, Grey Marl and Tea Green Marl to 460.42 m, Upper (Keuper) Marl to 906.25 m, Upper Sandstones (Keuper and Bunter) to 953.44 m, then Lower Sandstones (possibly Permian) to a final depth of 1,105.17 m.

The New Red Sandstone sequence of the Burton Row Borehole correlates well with that of the Puriton Borehole and the tentative classification of the strata is based on that of Ussher³. The Keuper Marl comprises purplish and brownish red siltstones, with green bands, patches and spots. Veins of pink rock salt were first encountered at 643 m depth and became abundant between 689 m and 693.76 m depth, where the Keuper siltstones had a spongy appearance. Bedded, colourless and pink rock salt, with varying proportions of siltstone, which sometimes predominated, were present between 693.76 m and 742.40 m depth. Halite veins and stringers occurred below the main saliferous horizons down to a depth of 797 m. Other evaporite minerals proved by the borehole include anhydrite and gypsum in small quantities.

In the Puriton Borehole the rock salt had a vertical range of about 36.6 m. Nearer the long axis of the Central Somerset

Basin, the Burton Row Borehole has shown the main salt beds to extend, vertically, through some 53 m of strata. The saliferous beds thus thicken into the basin but maintain the same relative stratigraphical position; this suggests that the saliferous beds are probably present, at depth, between the two borehole localities, and further that the salt deposits may be co-extensive, laterally, with the main Central Somerset Basin. This west-north-west trending structure is a major synclinal downwarp bounded on the north by the Mendip Hills and on the south by an east-south-east trending line passing approximately through the Bridgwater area. The basin stretches westwards beneath Bridgwater Bay and its eastern boundary is ill-defined.

The absolute limits of the basin have not been proved, but in the vicinity of Burnham-on-Sea alone the area beneath which rock salt can be expected to occur may be as great as 100 square miles (259 sq km). A conservative estimate of the reserves indicates that at least 13,000 million long tons of rock salt may be preserved, at depth, underlying that part of the basin shown in Fig. 1.

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¹ McMurtrie, J., *Proc. Somerset Archaeol. Nat. Hist. Soc.*, **57**, 25 (1911).

² Whittaker, A., *Proc. Somerset Archaeol. Nat. Hist. Soc.*, **114**, 96 (1970).

³ Ussher, W. A. E., *Proc. Geol. Ass.*, **22**, 246 (1911).

Possible Land Plants from the Middle Cambrian, Queensland

DURING study of phosphorites from the Georgina Basin of north-west Queensland, two fossil fragments, possibly stems of land plants, were discovered in insoluble residues from lime-phosphate rocks. The discovery is significant in being one of the very few of possible land plant remains in the early Palaeozoic.

The sample from which the acid insoluble residues were recovered comes from a locality about 1.5 miles north of Mt Murray, at about 21° 49' S, 139° 59' E. They were found in lime-phosphate rocks, of the Beetle Creek Formation¹, consisting of sand-sized phosphatic and carbonate allochems in carbonate cement. Solution in dilute acid releases the phosphatic allochems as insoluble residues. No sectioning or other destructive preparatory technique has been used to discover the structure of the material. We presume that the specimens are preserved as colophane, because they are similar in appearance to the remainder of the colophane particles in the insoluble residues. These residues from this and other samples from the locality contain a large and varied fauna, including the following forms: *Pagetia*, *Ptychagnostus*, seven new species of bradoriids, *Acrothele*, and many other fragments of organic remains. *Pagetia* and *Ptychagnostus* fix the upper age limit as Middle Cambrian. The fact that the rocks are laterally equivalent to beds a few miles to the south containing *Xystridura* fixes the age as lower Middle Cambrian. The rocks are overlain by the Devoncourt Limestone which contains a Middle Cambrian fauna (unpublished results by Shergold, J. H.).

Monopodial branching of the plant axes is the only reliable criterion suggesting that the remains might be vascular. Chaloner² regards this as only supporting evidence to show that similar remains are vascular, but the mode of preservation here is such that any evidence of his other criteria would have been destroyed.

The smaller fragment (Fig. 1a) is badly worn, but when viewed end-on a slight, outer rim is apparent, caused either by

fossilization or by original tissue differentiation. The better specimen (Fig. 1b and c) is flattened, with longitudinal striations on both sides; these suggest that it represents a compression where the central tissue collapsed, but the cortical tissue remained more or less undamaged until fossilization was complete. The cortex is not fractured along the folded margin; this may be additional evidence that a tougher cortex was present, as in the lower Silurian *Echostimella*, where Schopf³ suggested that a tougher cortex and less durable central conductive strands may have been present (he observed no evidence of tissue differentiation). It is not possible to suggest any identification for these remains. Various authors^{4,5} have pointed out that pre-Downtonian vascular plant-like remains are all very similar to Lower Devonian genera, and these fragments are no exception. *Dawsonites* has a similar surface ornamentation, but is branched dichotomously. Monopodial branching is rare in these primitive vascular plants. Lycopod-like remains of unknown affinity have been reported from the Cambrian of Eastern Siberia⁶ and the Ordovician of Bohemia⁷.

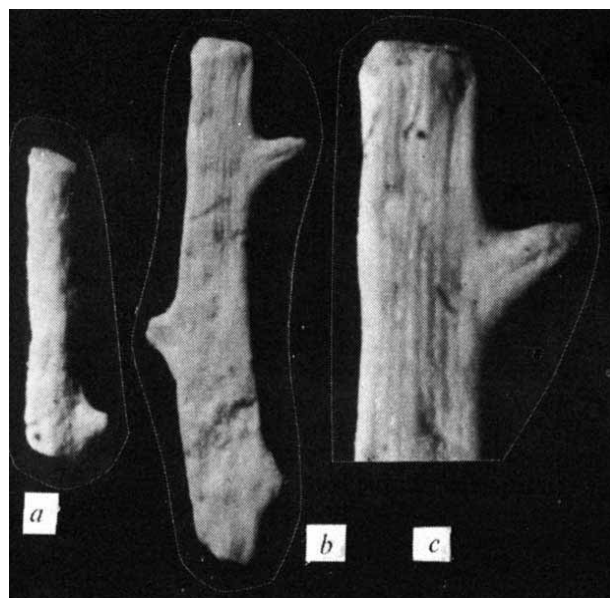


Fig. 1 Fragments of possible land plant stems. a, Fragment, 1.6 mm × 0.2 mm, showing a single branch, × 25; b, compressed fragment, 2.6 mm × 0.3 mm, with evidence of three branches; c, enlargement of Fig. 1b showing longitudinal striations which neither anastomose nor show nodal structures, and a rim suggesting tissue differentiation at the upper end, × 45.

Palynological evidence for the possible existence of pre-Silurian vascular plants is ambiguous, as spores with triradial scars can be produced by algae. Evidence from early Silurian spores strongly suggests that vascular plants existed, but Gray and Boucot⁸ in reporting them have urged caution in interpreting the evidence.

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¹ Russell, R. T., *Qd. Govt. Min. J.*, **68**, 153 (1967).

² Chaloner, W. G., *Biol. Rev.*, **45**, 355 (1970).

³ Schopf, J. M., *Prof. Pap. US Geol. Surv.*, **550**, D, D72 (1966).

⁴ Chaloner, W. G., *Biol. Rev.*, **45**, 356 (1970).

⁵ Meyen, S. V., *Trudy Geol. Inst. Akad. Nauk SSSR*, **208**, 37 (1970).

⁶ Krishtofovich, A. N., *Dokl. Akad. Nauk SSSR*, **91**, 1377 (1970).

⁷ Obrhel, J., *Vestn. Ustr. Ust. Geol.*, **43**, 463 (1968).

⁸ Gray, J., and Boucot, A. J., *Science*, **173**, 918 (1971).

Late Devonian *Cavellina* (Ostracoda) with Separate Receptacles for Eggs

A NUMBER of ostracods, *Cavellina lovatica* Zaspelova, with separate receptacles for eggs in the females' brood pouches, have been found during boring operations in the Upper Devonian deposits of the Malaja Vishera district, in the Novgorod region. In the specimens found, at a depth of 76.10 m, there were eleven valves, mostly well preserved; they were large (up to 1,225 μm long) and thin-walled. The brood chamber is separated by a well-marked ridge, running from the ventral to the dorsal margin, and gradually narrowing. Inside the chamber, very shallow, round cavities, which we believe to be receptacles for eggs, can be seen (Fig. 1). Some of these are very distinct, although others have somewhat obscured outlines; the walls between them are thickened. The number of receptacles in the valves varies from individual to individual (Table 1). From this it may be seen that the total number of eggs could be as much as 24, although this might vary with individuals between 16 and 24, and this number can differ between the left and the right valves of the same female. The size of these cavities varies between 100 and 120 μm , and this figure might approximate to the diameter of the eggs.

the eggs of recent Cytherelloidea. The two pits in the posterior part of the females are believed to be brood cavities⁸. We can assume that the Cytherelloidea lay up to four eggs. Perhaps the same number was laid by the Cytherelloidea in the past. This may be confirmed by the presence of two receptacles in many fossilized females of the Cytherelloidea, from Eocene⁸, Maestrichtian⁹, Hauterivian⁸, and Liassic¹⁰. The Anisian *Recytelloidea egorovi*¹¹ has a common chamber without separate cavities.

We should like to draw attention to the size of the brood chamber in *Cavellina*. The length of the chamber in *C. lovatica* is 300–360 μm . In the Lower Carboniferous cavellinids we have studied, the brood chamber is generally 250–300 μm long although we have encountered species where it was as short as 150–200 μm . In the cytherellids the brood chamber is even shorter. Our observations on the Triassic and some subsequent Cytherelloidea have revealed lengths of 125–150 μm . Thus in the course of geological time there has been a decrease in the size of the brood space in the Platycopa.

Our observations provide direct evidence for the existence in Devonian times of cavellinids with up to 24 eggs. We consider that in the course of their evolution the Platycopa have shown a three-fold decrease in the numbers of eggs brooded. To maintain their existence, the Platycopa, like other animal

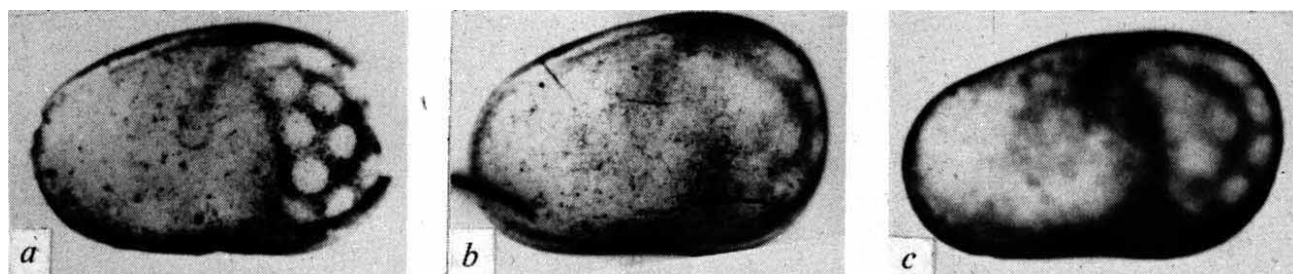


Fig. 1 Valves of *Cavellina*, for example, *lovatica*, with cells for eggs in transmitted light. *a* and *b*, Right valves from inside; *c*, left valve from outside. $\times 48$.

This discovery sheds some light on the number of eggs found in representatives of Platycopa, and on the evolution of breeding in this suborder, which comprises two families, Cavellinidae (Silurian-Triassic) and Cytherellidae (Triassic-Recent), the former being the ancestors of the latter^{1–4}.

The Cytherellidae belong to those groups of recent ostracods which characteristically carry their eggs within the valves of the carapace. This is a form of reproductive behaviour peculiar to animals with low fecundity. A few observations upon *Cytherella* have revealed that females lay their eggs within the carapace and they are retained within the posterior part which functions as a brood chamber. This is sometimes separated from the anterior space by a short bar. All the eggs of one brood are laid approximately at the same time and simultaneously undergo the embryonic stages up to hatching⁵. The number of eggs observed varies rather greatly: *Cytherella abyssorum*—an average of 7⁵, *C. serrulata*—8⁶, *C. arostrata*—4⁷. In the brood chambers of *Cytherella* there are usually no receptacles for eggs; only in *C. arostrata* has the chamber two cavities, each containing one egg⁷. There are no data about

groups¹², developed improved methods of brood rearing, so as to increase the survival rate of their offspring. Thus reproductive efficiency was achieved by a reduction of brood size, correlated with morphological changes, such as a reduction in the size of the brood chamber, and possibly by a general decrease in the size of the carapace. These changes, together with those associated with the biserial adductor muscle scar, are the main historical features of the suborder. The diminution of breeding was, probably, an ancient and a complicated process, which has developed in several separate lines. The decrease in the brood size could occur as a result of the combined actions of, first, variability, which produced females with smaller brood chambers and fewer eggs (which, possibly, gave some adaptive advantage, for example, facilitating locomotion) and, second, selection.

This shows the vital importance of the reproductive process in the evolution of the Platycopa. We believe that, for a better understanding of the evolution of the ostracods, the attention of students should be drawn to the problems of reproduction. It may be supposed that important changes in the structure of ostracods during the Late Palaeozoic-Triassic, which resulted in the extinction of the Palaeocopida and brought about the dominance of the Podocopa, also included changes in reproductive behaviour. The types of sexual dimorphism in the Palaeocopida^{13,14} indicate the widespread occurrence of egg brooding. But the elaborate and highly-specialized structures obviously became an obstacle to the further development of the group; for example, there might be difficulties in copulation, complications in transferring the eggs to the pouches, or even hindrance to locomotion. It might be that, during the Palaeozoic, there was a high incidence of egg-brooding, and this was followed, in the Mesozoic and Cainozoic

Table 1 Variation of Number of Receptacles in Left and Right Valves

No. of receptacles	Occurrence in valves	
	Left	Right
12	2	1*
10	1	3†
9	1	—
8	1	—

* See Fig. 1a.

† See Fig. 1a and b.

periods, by an increase of breeding without parental care, with attendant laying rather than bearing of eggs, an evolutionary degeneration to an earlier pattern of behaviour.

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Received November 24, 1971.

- ¹ Egorov, V. G., *Ostracody frnskogo jarussa Russkoj Platformy* (I. Kloedenellidae, Gostopetkhisdad, Moskva, Leningrad, 1950).
- ² Osnovy Paleologii, Czlenistonogije, *Trilobitoobrasnye i Rakoobrasnye* (Gosgeoltekhisdat, Moskva, 1960).
- ³ Geol. Soc. Amer., *Treatise on Invertebrate Paleontology*, Q, Arthropoda 3 (Kansas Univ. Press, Lawrence, Kansas, 1960).
- ⁴ Gramm, M. N., *Iskopajemaja fauna i flora Dalnego Vostoka*, 41 (Vladivostok, 1969) (in Russian).
- ⁵ Elofson, O., *Zool. Bidr. Upps.*, 19, 215 (1941).
- ⁶ Brady, G. S., and Norman, A. M., *Sci. Trans. Roy. Dublin Soc.*, Series 2, 5, 621 (1896).
- ⁷ Kornicker, L. S., *Micropalaeontology*, 9, 61 (1963).
- ⁸ Van Morkhoven, F. P. C. M., *Post-palaeozoic Ostracoda*, 2 (Elsevier, Amsterdam, 1963).
- ⁹ Van Veen, J. E., *Verh. Geol. Mijnb. Genootsch. Nederland en Kolonien*, 9, 317 (1932).
- ¹⁰ Field, R. A., *Senckenbergiana Lethaea*, 51, 87 (1966).
- ¹¹ Gramm, M. N., *Dokl. Akad. Nauk. SSSR*, 173, 931 (1967) (in Russian).
- ¹² Schmidt, G. A., *Usp. Sovrem. Biol.*, 14, 160 (1941) (in Russian).
- ¹³ Ivanova, V. A., in *Itogi nauki, Stratigraphija, Paleontologija*, 1967, 181 (Viniti, Moskva, 1968) (in Russian).
- ¹⁴ Kesling, R. V., *Contrib. Mus. Paleontol. Univ. Mich.*, 22, 273 (1969).

lent number of photons in the presence of other gases. This calculated lifetime was then increased by $\times 16$; the ratio of the area of the surface of a sphere to its cross-sectional area is 4 and the quantum yield for ammonia photolysis 0.25 (refs. 9, 10).

Table 1 Calculated Lifetimes for Ammonia Photolysis

	Aqueous NH ₄ ⁺ (molarity) *	Potential atmospheric gases (torr) †					NH ₃ lifetime (years $\times 10^6$)
		NH ₃	H ₂ O	CH ₄	H ₂ S	CO ₂	
1	1	0.51	0.76	1.3	0	—	0.4
2	10 ⁻²	0.0051	0.76	1.3	0	—	0.6
3	10 ⁻²	0.0051	0.76	13	0	—	0.6
4	10 ⁻⁴	0.000051	0.76	1.3	0	—	1.8
5	10 ⁻²	0.0051	0.76	0	0	—	0.6
6	10 ⁻²	0.0051	2.4 ‡	130	—	—	0.6
7	10 ⁻²	0.0051	7.6	130	—	—	0.6
8	10 ⁻²	0.0051	24 §	130	—	—	0.6
9	10 ⁻²	0.0051	0.76	130	—	1	0.6
10	10 ⁻²	0.0051	0.76	130	—	100	0.6
11	10 ⁻²	0.0051	0.76	130	0.00063	—	1.4
12	1	0.51	0.76	13	0.0063	—	0.6
13	10 ⁻²	0.0051	0.76	13	0.0063	—	4
14	10 ⁻²	0.0051	0.76	130	0.063	—	26
15	10 ⁻²	0.0051	0.76	130	0.63	—	220
16	10 ⁻²	0.0051	0.76	130	6.3	—	2,000

* Bada and Miller⁴ calculated that the NH₄⁺ concentration would be 10⁻²–10⁻³ M.

† We assumed that the remainder of the atmosphere consisted of inert gases which did not have significant ultraviolet absorption.

‡ Assuming a relative humidity of 50% at 0° C.

§ Assuming a relative humidity of 100% at 25° C.

Table 1 shows that when the partial pressure of ammonia in the atmosphere is decreased its lifetime is increased (compare 1 and 4 in Table 1). The shortest lifetimes calculated are still ten times greater than Abelson's value of 3×10^4 yr (ref. 8); however, only one of the values exceeds 10^9 yr (the age of the Earth is about 4.5×10^9 yr).

Water vapour exerts a negligible protective effect on ammonia (compare 2 and 8, Table 1) despite extensive UV absorption from 190–100 nm. This range represents only 2.5% of the total solar output in the 230–100 nm region where ammonia absorbs light.

We assumed that an atmosphere containing H₂S would reduce ammonia photolysis because of the intense absorption of H₂S in the 240–100 nm region where ammonia also absorbs light. We found, however, that a constant pressure of at least 6.3 torr H₂S ($\times 1,000$ the maximum ammonia content⁴) is required to protect ammonia for 2×10^9 yr (Table 1).

H₂, CO, CO₂, CH₄, N₂, and HCl have little or no absorption in the 230–190 nm spectral region and, as shown in Table 1 for CO₂ and CH₄, would not have prevented the photodecomposition of ammonia.

Our calculations did not consider chemical reactions between photochemically excited molecules and other atmospheric constituents. We therefore measured the quantum yield for ammonia photodecomposition in the presence of other potential constituents of the atmosphere of the primitive Earth. The gaseous mixtures were irradiated using an iodine lamp with principal emission at 206.2 nm^{11–13} and the observed quantum yield was compared with that for the photolysis of a standard mixture of ammonia and argon using the same reaction conditions, with a quantum yield of 0.25.

Hydrogen was the only gas which markedly decreased the decomposition of ammonia (Table 2), but only at pressures greater than 50 torr (Fig. 1). Approximately the same pressure of hydrogen is needed to inhibit the photolysis of either 10 torr or 1 torr of ammonia, indicating that this inhibition is independent of the ammonia pressure. We found that H₂S, CO and O₂ all accelerate ammonia decomposition (Table 2). The quantum yields for the former two gases are tentative because solid reaction products coated the windows of the photolysis cells.

Ammonia Photolysis and the Role of Ammonia in Chemical Revolution

The suggestion that the primitive atmosphere was highly reducing and consisted mainly of methane, ammonia and water vapour¹ is supported by Miller's observation that amino-acids are formed by electrical discharges through such a mixture² and the synthesis of various biomolecules under presumed primitive Earth atmospheres containing ammonia³. Bada and Miller⁴ point out that an ammonium ion concentration of 10⁻² to 10⁻³ M is necessary for the synthesis of these biomolecules while Rasool and McGovern⁵ suggest that a methane-ammonia atmosphere could have been maintained for 10^9 years by a low leakage rate of hydrogen.

If the atmosphere of the primitive Earth was formed by volcanic outgassing it would have contained very little methane and ammonia because these gases are not found in the effluent of contemporary volcanoes^{6–8}. It has been claimed that any ammonia present would have been photolysed in 3×10^4 years or less by ultraviolet (UV) light⁸.

We have investigated photodestruction of ammonia on the primitive Earth. Abelson⁸ did not consider that the ammonia would be present mainly as dissolved ammonium ions which would not be subject to photochemical decomposition⁴ and he neglected the effects of other constituents of the primitive atmosphere, either in protecting ammonia from photodestruction by absorbing UV light, or by reacting with photoexcited intermediates to regenerate the ammonia.

We devised a computer program to calculate the time needed to destroy ammonia photolytically if all the nitrogen in the contemporary atmosphere had been present as ammonia or ammonium salts. The program inputs were the Sun's spectral energy output at 1 nm intervals from 100–400 nm and the absorbances of the possible atmospheric constituents at 1 nm intervals. With hypothetical potential primitive atmospheres we calculated the time taken for ammonia to absorb an equivalent

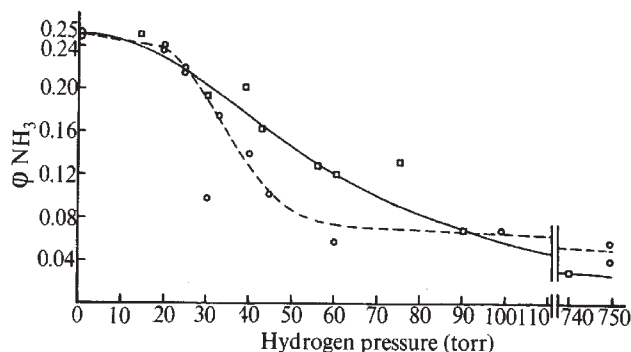


Fig. 1 Variation in the quantum yield (ϕ) for ammonia photolysis with hydrogen pressure. —, 10 torr ammonia; ---, 1 torr ammonia.

We conclude that ammonia did not have an important role in chemical evolution. Only large amounts of H_2S (>1 torr) or hydrogen (>50 torr) could have preserved the ammonia. Estimates of the hydrogen pressure on the primitive Earth range from 7.6 torr to 7.6×10^{-6} torr (refs. 4, 16–18), values considerably less than 50 torr. The pressure of H_2S would probably be less than 1 torr through photochemical destruction and precipitation by metal ions. Other UV light absorbing gases such as ozone may have been present in an oxidizing atmosphere, but significant amounts of ammonia could not have existed under oxidizing conditions.

Table 2 Effect of Other Gases on the Quantum Yield of Ammonia Photolysis

	NH_3 *	Gas A *	Gas B *	ϕNH_3
1	12.5	CH_4 736.5		0.25
2	9.0	CO_2 92.0	Ar 660	0.23
3	11.0	H_2O 21.2	Ar 714.8	0.16
4	20.0	He 737.4		0.25
5	52	H_2S 0.45	Ar 708	$\sim 0.5^\dagger$
6	14.4	CO 743.1		$\sim 1^\dagger$
7	14.7	N_2 572	O_2 150	0.85
8	14.5	H_2 740		0.01

* Concentration is given in pressure (torr).

† Precipitate formed in the irradiation cell.

Alternatively an appreciable steady state concentration of ammonia would have been maintained if the rate of ammonia synthesis equalled the rate of photodestruction. This is unlikely because it has been estimated that the UV light energy greatly exceeded the energy sources, such as thermal or electrical discharge, which might have affected synthesis of ammonia¹⁹.

We thank Professors R. Reeves and P. Hartek for assistance. This work was supported by a NASA research grant and an NIH career development award.

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Received March 6, 1972.

- 1 Urey, H. C., *Proc. US Nat. Acad. Sci.*, **38**, 351 (1962).
- 2 Miller, S. L., *J. Amer. Chem. Soc.*, **77**, 2351 (1955).
- 3 Lemmon, R. M., *Chem. Revs.*, **70**, 95 (1970).
- 4 Bada, J. L., and Miller, S. L., *Science*, **159**, 423 (1968).
- 5 Rasool, S. I., and McGovern, W. E., *Nature*, **212**, 1225 (1966).
- 6 Rubey, W. W., *Geol. Soc. Amer. Spec. Paper*, **62**, 363 (1955).
- 7 Cloud, P. E., *Science*, **160**, 729 (1968).
- 8 Abelson, P. H., *Proc. US Nat. Acad. Sci.*, **55**, 1365 (1966).
- 9 Noyes, W. A., and Leighton, P. A., *The Photochemistry of Gases*, 374 (Dover, New York, 1966).
- 10 Brandt, J. C., *The Physics and Astronomy of the Sun and Stars* (McGraw-Hill, New York, 1966).
- 11 Hartek, P., Reeves, jun., R. R., and Thompson, B. A., *Z. Naturforsch.*, **19a**, 2 (1964).
- 12 Thompson, B. A., Reeves, jun., R. R., and Hartek, P., *J. Phys. Chem.*, **69**, 3964 (1965).

- 13 Buschmann, N. W., and Groth, W., *Ber. Busenbes. Physik. Chem.*, **73**, 859 (1969).
- 14 Calvert, J. G., and Pitts, jun., J. N., *Photochemistry*, 782 (John Wiley, New York, 1966).
- 15 Urey, H. C., *The Planets, Their Origin and Development* (Yale University Press, New York, 1952).
- 16 Holland, H. D., in *The Origin and Evolution of Atmospheres and Oceans* (edit. by Brancazio, P. J., and Cameron, A. G. W.), 86 (John Wiley, New York, 1964).
- 17 Miller, S. L., and Urey, H. C., *Science*, **130**, 245 (1959).
- 18 Brinckman, R. T., *J. Geophys. Res.*, **74**, 5355 (1969).
- 19 Korowitz, N. H., and Miller, S. L., *Fortschr. Chem. Org. Natstoffe*, **20**, 432 (1962).

BIOLOGICAL SCIENCES

Ribosomal Proteins: Variation of the Protein Composition in *Escherichia coli* Ribosomes as Function of Growth Rate

PURIFIED 30S *Escherichia coli* ribosomal subunits are heterogeneous *in vitro*^{1,2} both structurally and functionally, but there has been no experimental evidence of a corresponding heterogeneity *in vivo*. To test this possibility we studied the protein composition of ribosomes synthesized by bacteria under different growth conditions.

We grew bacteria in rich (yeast extract and peptone) or in minimal (M9 modified³) medium, and labelled the cells with different isotopes (¹⁴C or ³H amino-acids). The cells harvested in middle log phase were mixed before grinding and the ribosomes were isolated. Ribosomal proteins were extracted and separated on polyacrylamide slabs by two-dimensional gel electrophoresis⁴. After staining, the protein spots were cut out and burned under oxygen in a Packard sample oxidizer which separates ³H from ¹⁴C. The d.p.m. values were determined in a scintillation counter with automatic quench control; details of the method will be given elsewhere (E. D., manuscript in preparation).

Six experiments with several polyacrylamide slabs in each experiment were carried out, and for each ribosomal protein the following ratio was determined: d.p.m. for one isotope corresponding to rich medium to d.p.m. for the other isotope corresponding to minimal medium. The proteins can be grouped into four classes with respect to their ratios: about two-thirds of all proteins gave ratios between 0.90 and 1.10. A rather large group (S1, S10, S11, S19, S20 from 30S subunits and L8+L9, L17, L27, L32, L33 from 50S) had ratios which were slightly but not always reproducibly different from those of the first group. For proteins L7 and L16 the ratios were 0.8. The ratios for three proteins, namely 3.1 for protein L12, 2.5 for S6 and 2.4 for S21, differ considerably from all the others. Controls were performed in exactly the same way as described above, but the parallel cultures were grown in identical media (rich/rich or minimal/minimal, respectively). In these experiments the ratios were 1.0 ± 0.1 for all ribosomal proteins.

Each of the three proteins (S6, S21 and L12) with the greatest variance has been analysed for its function. Protein S6 is involved in the binding of fMet-tRNA. Omission of this protein during 30S reconstitution results in a distinct reduction of AUG and F₂ dependent fMet-tRNA binding⁵. Protein S21 is a fractional protein (ref. 2 and Weber, H. J., manuscript in preparation) and its addition to ribosomes strongly inhibits the F₂ dependent binding of fMet-tRNA⁶. The structure of L12 is almost identical to that of L7 as shown by chemical and immunological studies^{7–11}. The only difference so far found between them is the presence (L7) or absence (L12) of an acetyl group at the N-terminus¹².

Stoichiometric studies (ref. 10 and P. Thammana *et al.*, in preparation) show that the sum of L7 and L12 is 2 to 3 copies per ribosome, and that the ratio between them varies with growth conditions. Both proteins are involved in the G-factor dependent GTPase activity¹³.

At present it is hard to give a clear explanation for these results. Nevertheless, slightly different treatment of ribosomes during the isolation procedure is excluded by mixing the double-labelled cells before grinding. We cannot, however, exclude the possibility that as a result of physiological conditions in cells grown in different media, some ribosomal proteins respond differently to identical extraction conditions. If this were not the case, our findings would imply that populations of ribosomes with quantitatively different sets of proteins can be demonstrated *in vivo*, and would support the biological significance of the heterogeneity of a ribosomal population so far only shown *in vitro*.

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- ¹ Kurland, C. G., Voynow, P., Hardy, S. J. S., Randall, L., and Lutter, L., *Cold Spring Harbor Symp. Quant. Biol.*, **34**, 17 (1969).
- ² Voynow, P., and Kurland, C. G., *Biochemistry*, **10**, 517 (1971).
- ³ Apirion, D., *J. Mol. Biol.*, **16**, 285 (1966).
- ⁴ Kaltschmidt, E., and Wittmann, H. G., *Analyt. Biochem.*, **36**, 401 (1970).
- ⁵ Nomura, M., Mizushima, S., Ozaki, M., Traub, P., and Lowry, C. V., *Cold Spring Harbor Symp. Quant. Biol.*, **34**, 49 (1969).
- ⁶ van Duin, J., van Knippenberg, P. H., Dieben, M., and Kurland, C. G., *Molec. Gen. Genetics*, **116**, 181 (1972).
- ⁷ Kaltschmidt, E., Dzionara, M., and Wittmann, H. G., *Molec. Gen. Genetics*, **109**, 292 (1970).
- ⁸ Möller, W., Castleman, H., and Terhorst, C. P., *FEBS Letters*, **8**, 192 (1970).
- ⁹ Mora, G., Donner, D., Thammana, P., Lutter, L., and Kurland, C. G., *Molec. Gen. Genetics*, **112**, 229 (1971).
- ¹⁰ Möller, W., Groene, A., Terhorst, C., and Amons, R., *Europ. J. Biochem.*, **25**, 5 (1972).
- ¹¹ Stöffler, G., and Wittmann, H. G., *J. Mol. Biol.*, **62**, 407 (1971).
- ¹² Terhorst, C., Wittmann-Liebold, B., and Möller, W., *Europ. J. Biochem.*, **25**, 13 (1972).
- ¹³ Kisch, K., Möller, W., and Stöffler, G., *Nature*, **233**, 62 (1971).

***In vitro* Culture of Rabbit Ova fertilized by Epididymal Sperms in Chemically Defined Media**

CAPACITATION of hamster^{1,2} and mouse³ sperms *in vitro* has been achieved in the presence of, or after treatment by, follicular fluid. *In vitro* fertilization of mouse eggs by epididymal sperms^{4,5} can take place in a synthetic medium without follicular fluid. These findings indicate that the current concept of capacitation should be modified. Confirmation of the results might be found in rabbit ova and sperms, because the capacitation of rabbit sperms is generally accepted as necessary for fertilization.

We describe the successful *in vitro* fertilization of rabbit ova by epididymal sperms in synthetic medium, and the results of culturing the fertilized ova *in vitro* to the blastocyst stage.

An established combined medium⁶ was slightly modified; sodium caseinate solution was replaced by 60% v/v Ham F₁₂ solution⁷. It was adjusted to pH 7.5 with NaHCO₃, and 60 mg of kanamycin sulphate/l⁸ was added. The active motility of epididymal sperms was retained in this medium for more than 5 h at 37° C, and it was therefore used for the *in vitro* insemination. For cultivation of the ova after *in vitro* fertilization, the medium was supplemented with 20% v/v

calf serum, 100 mg/l. of sodium pyruvate, and 40 µg of thiamine propyl disulphide/l.

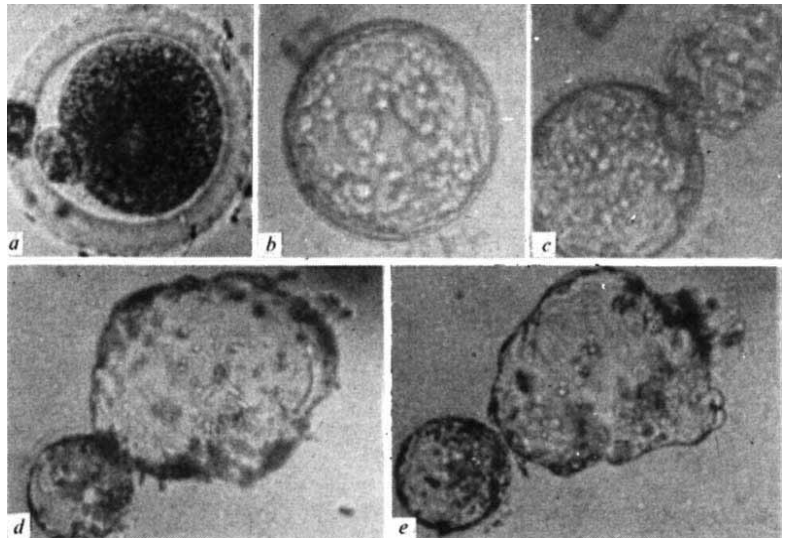
Ovulation was induced by single injection of 100 IU of human chorionic gonadotrophin (HCG). The ova were flushed from the oviducts with 4 ml. of the medium 17–19 h after the injection. The spermatozoa used for the *in vitro* insemination were taken from the epididymus. Fertile males received a pretreatment of a single intravenous injection of 100 IU HCG. Our earlier work showed that this treatment yielded a high quality epididymal semen for artificial insemination. Forty-eight hours after the injection, a piece of epididymal tail was removed surgically, and transferred into 2 ml. of the medium in a Petri dish which was immediately agitated to prevent coagulation of sperms and kept at 37° C in a humidified incubator in 5% CO₂ in air for 10–20 min. The concentrated sperm suspension was transferred by a sterilized pipette to a watch glass containing 3 ml. of medium, giving a sperm cell concentration of about 2–4 × 10^{7–8} ml. Groups of five eggs with cumulus oophorus were placed in the sperm suspension. As a control, one group of ova was placed in the medium without sperm cells. The system was incubated for 5 h in the CO₂ incubator, and the eggs were then transferred by capillary to hole glasses (hole diameter 3.5 cm, depth 5 mm) containing 3 ml. of the culture medium, each glass receiving three eggs. The glass hole was protected with a coverslip, and the edges were sealed together with sterilized paraffin. The eggs were then cultured beyond the 2-cell stage for 6 days at 37° C. The concentration of sperm cells caused turbidity and made it impossible to observe the eggs microscopically. The ova were therefore examined for fertilization after transferring from the sperm suspension into the culture medium. They were checked three times, at intervals of 3 h from the start of cultivation, by phase contrast microscopy. The development of embryos in the culture medium was checked daily by inverted microscopy, and classified according to the latest stage reached. A microcinematographic microscope was also used to record continuously the behaviour of some eggs during cultivation. The criteria used to determine *in vitro* fertilization were the formation of two polar bodies and the presence of pronuclei undergoing fertilization.

No formation of two polar bodies was found in the control embryos, and the incidence of cleavage in this group was rare. Of a total of 89 control ova, only seven embryos showed 2 to 5-cell cleavage, indicative of spontaneous fluctuation as the division of cells was not symmetrical, and no further cleavage was found.

In the group which had been kept in medium containing a large number of sperms, a high percentage of the ova showed signs of complete fertilization. Sixty-seven out of 113 ova incubated seemed to have undergone fertilization and early cleavage. Thirty-six of these fertilized ova attained 2 to 8-cell stages, but thereafter remained at these same stages or collapsed. The other thirty-one ova developed more frequently to blastocyst (twenty-seven ova) than to morula (four ova). Hatching of the blastocysts was observed in nineteen specimens (28%). The embryos expanded further after hatching. Time lapse microcinematographs (1 frame every 2 min) of the embryo, taken from the onset of cultivation after recovery from the sperm suspension, show a regular pattern of cleavage and the hatching process (Fig. 1). In these specimens, the formation of blastocysts paralleled that reported earlier.

In view of the fact that the capacitation of ejaculated sperm cells normally takes place in the female genital tract^{8,9} or in some body fluids^{1–3,10,11}, the *in vitro* fertilization of rabbit ova with epididymal spermatozoa might be expected to be almost impossible to complete in a synthetic medium. Cleavage and development found in this study were, however, comparable with those observed elsewhere⁶ in the culture of fertilized ova, whereas the group of ova kept in the medium without sperms showed no signs of fertilization or of normal cleavage. We conclude that the medium employed can be used both for *in vitro* insemination and for culture of the ova from the one-cell

Fig. 1 Development of rabbit ova following *in vitro* fertilization by epididymal spermatozoa. From a time lapse film (16 mm, 1 frame every 2–5 min) of an ovum in a culture medium after isolation from sperm suspension. *a*, Stage of two polar bodies, 30 min after the onset of cultivation ($\times c. 180$). *b*, Blastocyst stage, 135 h after *a* ($\times c. 120$). *c*, Hatching stage, 10 h after *b* ($\times c. 120$). *d*, Late stage of hatching, 3.5 h after *c* ($\times c. 90$). *e*, Blastocyst after hatching, 4 h after *d* ($\times c. 90$).



stage to the hatching stage through the complete formation of the expanding blastocyst. It is surely not unreasonable to suggest that the concept of capacitation should be radically changed. We suggest that our results indicate that incubation in a synthetic medium causes rabbit sperms to develop an increased capacity for fertilization. We also suggest that the hormonal pretreatment of the male rabbit (a single injection of HCG) had a favourable effect on the sperms, allowing them to complete *in vitro* fertilization of ova. A large quantity of medium with a high concentration of sperm cells was used in this study. These conditions might also be effective, affording special conditions for the removal of corona cells and providing favourable conditions for sperm entry into the ova. Much work has been done on the storage of sperm and the maintenance of sperm life by lowering temperature, but few attempts have been made to maintain the active motility of the cells at body temperature. The first step in the approach to complete fertilization of mammalian ova *in vitro* appears to be to obtain highest quality semen and to find a suitable medium in which to maintain the active motility of sperms for at least several hours at body temperature. Pretreatment of the male animals with HCG seems effective in obtaining the required standard of sperm cells.

This work was supported by research grants from the Ministry of Education, Japan, and from Nihon University.

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Received March 13, 1972.

- ¹ Barros, C., and Austin, C. R., *J. Exp. Zool.*, **166**, 317 (1967).
- ² Yanagimachi, R., *J. Exp. Zool.*, **170**, 269 (1969).
- ³ Iwamatsu, T., and Chang, M. C., *J. Exp. Zool.*, **175**, 271 (1970).
- ⁴ Toyoda, Y., Yokoyama, M., and Hoshi, T., *Jap. J. Anim. Reprod.*, **16**, 147 (1971).
- ⁵ Toyoda, Y., Yokoyama, M., and Hoshi, T., *Jap. J. Anim. Reprod.*, **16**, 152 (1971).
- ⁶ Ogawa, S., Satoh, K., and Hashimoto, H., *Nature*, **233**, 422 (1971).
- ⁷ Ham, R. G., *Proc. US Nat. Acad. Sci.*, **53**, 288 (1965).
- ⁸ Austin, C. R., *Austral. J. Sci. Res.*, Ser. B, **4**, 581 (1951).
- ⁹ Chang, M. C., *Nature*, **168**, 697 (1951).
- ¹⁰ Noyes, R. W., Walton, A., and Adams, C. E., *J. Endocrinol.*, **17**, 374 (1958).
- ¹¹ Belford, J. M., *Advances in the Biosciences* (edit. by Raspé, G.), **4**, 35 (Pergamon Press, London, 1969).

Effect of Calcitonin on Vitamin D Metabolism

VITAMIN D is converted by the liver to the major circulating form, 25-hydroxycholecalciferol (25-HCC)¹, and further hydroxylated by the kidney² to a more active metabolite, 1,25-dihydroxycholecalciferol (1,25-DHCC)^{3,4}. The physiological mechanisms controlling this new renal endocrine function are still largely unknown, although both diet⁵ and parathyroid hormone^{6,7} have an influence. We report here experiments which show that calcitonin dramatically enhances production of 1,25-DHCC by the kidney. Our results have important physiological implications for understanding of calcium metabolism and may also have practical consequences in the choice of treatment for Paget's disease.

Inbred Wistar rats (40–50 g) of both sexes (Carworth Europe) were born of vitamin-D-deficient mothers, and maintained since weaning on a non-rachitic D-deficient diet (Ca 0.72%, P 0.35%). Synthetic salmon calcitonin was obtained from Sandoz Limited, Basle, Switzerland, with a potency in the rat bioassay of 3,570 MRC units mg⁻¹. 25-Hydroxycholecalciferol (26-(27-methyl-³H)-25-hydroxycholecalciferol (13.1 Ci/mmol) was from the Radiochemical Centre, Amersham.

Forty-eight rats were divided into three equal groups, and fed the D-deficient diet enriched with calcium carbonate to calcium concentrations of 1%, 1.5% and 2.0% respectively. On the fourteenth day each diet group was further subdivided into 4 subgroups of 4 rats; one group served as control for each diet. The other three subgroups of each diet group were given synthetic salmon calcitonin (0.25, 1.0 and 4.0 µg per 24 h) by 6 hourly subcutaneous injection. 3.5 h after the eighth calcitonin injection (48 h pretreatment) 1 µCi (30.6 ng) of labelled 25-HCC was injected intravenously in 0.1 ml. D-deficient serum into the tail vein of each rat. Further calcitonin was given at 2.5 and 8.5 h after 25-HCC. The rats were bled by aortic puncture under ether anaesthesia 1, 4, 8 and 12 h after the injection of 25-HCC. Serum and intestinal mucosa (18 cm from the pyloric sphincter) were collected from each rat, lyophilized and stored at -70° C. Sera (0.8 ml.) and mucosa were extracted individually and chromatographed on 'Sephadex LH20', as described previously⁶.

Extreme variations in dietary calcium have been shown to influence the type of metabolite produced (ref. 5 and our unpublished results), but our three diet groups could not be distinguished and results were therefore pooled. As shown previously⁶, chromatography on 'Sephadex LH20' separated the radioactive components in the serum and mucosal extracts into three main peaks. These were: peak IV, Va and peak V

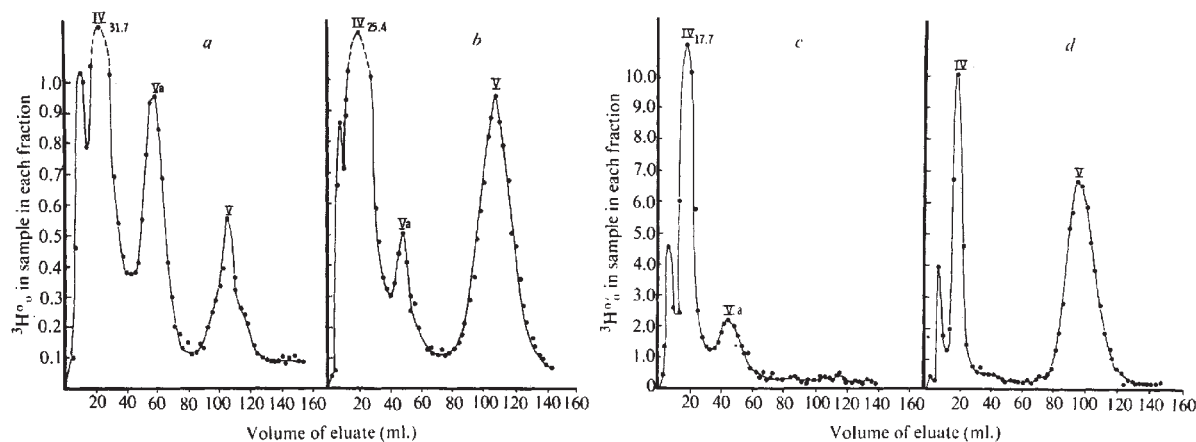


Fig. 1 Chromatography on 'Sephadex LH20' of extracts of serum and gut mucosa from D-deficient rats. Each trace is from one rat typical of its subgroup. *a*, Control rat, serum; *b*, rat receiving 0.25 µg calcitonin per 24 h, serum; *c*, control rat, mucosa; *d*, rat receiving 0.25 µg calcitonin per 24 h, mucosa. *a* and *b* were at 12 h and *c* and *d* at 8 h after ^3H -25-HCC, respectively.

presumably representing 25-HCC, 24,25-DHCC* and 1,25-DHCC respectively. The same three major peaks could be identified in the extracts from gut mucosa (Fig. 1).

Effects produced by calcitonin were considerable: peak V was greatly increased and peak Va diminished or abolished. This was seen 1, 4, 8 and 12 h after 25-HCC administration in the serum and 8 and 12 h in the gut (Figs. 1, 2 and 3). These are very gross changes and demonstrate conclusively that calcitonin has a powerful effect on vitamin D metabolism.

Despite continued large doses of salmon calcitonin, serum calcium values returned to normal after 48 h (Fig. 4), although controls showed marked hypocalcaemia in the first 24 h of calcitonin administration. A similar adjustment is seen in patients with Paget's disease after treatment with calcitonin⁸.

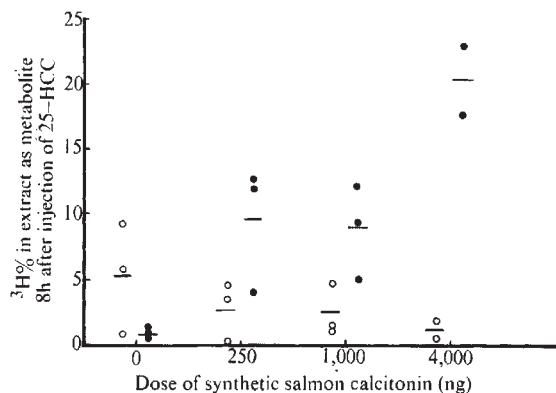


Fig. 2 Effect of salmon calcitonin on metabolites of 25-HCC in serum. 0.8 ml. of serum taken 8 h after 25-HCC from each of the three rats in each dose group was extracted and chromatographed. One rat in the 4 µg dose group died. Similar results are seen at 1 (less marked), 4 and 12 h. ○, 24,25-DHCC; ●, 1,25-DHCC.

Our results suggest that calcitonin enhances production of 1,25-DHCC by the kidney and suppresses that of 21,25-DHCC. This action is opposite to that produced by parathyroid extract⁶ and similar to the effect of a very low calcium diet (ref. 5 and our unpublished results). It is uncertain⁷ whether the effect of diet is due to the accompanying serum calcium changes, and possibly the hypocalcaemia in the first 24 h explains our findings. Parathyroid extract, however, exerts its effect without serum calcium changes and we suggest that this new action of calcitonin is due at least in part to direct action of the hormone on a renal target cell. The controlling factor in the type of metabolite produced is probably, in part, the intracellular calcium concentration⁶ and it

* DeLuca (personal communication) finds that peak Va, formerly identified as 21,25-DHCC, is in fact 24,25-DHCC.

seems likely that calcitonin lowers this concentration in the kidney cell. Such an effect of calcitonin has been suggested in the case of the target cells in bone^{9,10}. These results with our previous studies show for the first time that calcitonin, parathyroid hormone and vitamin D are directly inter-related. The physiological implications are not clear, especially as the action of 1,25-DHCC is known only in outline, while that of 24,25-DHCC has scarcely been studied. Confirmation with other synthetic calcitonins is required, although our findings will probably be reproduced with hormones from other species. One intriguing possibility raised is that we may now have a clue to the unknown function of the large amounts of calcitonin present in cartilaginous fish. Virtually nothing is known of D metabolism in primitive vertebrates and the possibility that calcitonin is involved is worth investigation.

The practical consequences of our results are more immediately apparent. First, they provide an explanation for the enhanced intestinal absorption of calcium during calcitonin treatment of Paget's disease⁸: this may be partly due to increased accumulation of 1,25-DHCC in the gut mucosa under the influence of calcitonin. Second, they are relevant to the long-term treatment of patients with calcitonin. Diphosphonates have been shown to influence the course of Paget's disease¹¹, but there is concern at the observation that these drugs may produce osteomalacia¹². Stanbury and colleagues explained this finding by showing that diphosphonates block the production of 1,25-DHCC in the kidney¹³. Calcitonin has the reverse effect and should be free from the risk of

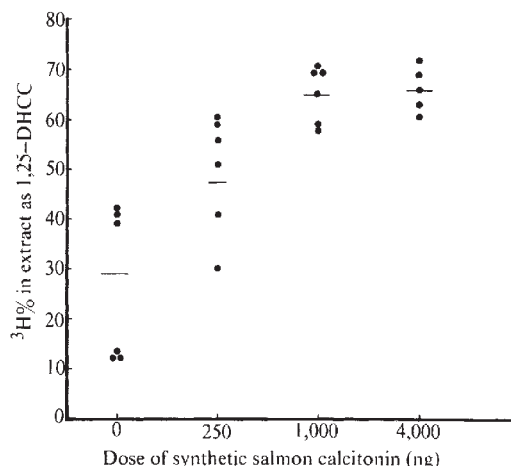


Fig. 3 Effect of salmon calcitonin on ^3H % as 1,25-DHCC in extracts of gut mucosa. Each point represents one rat. The values at 8 and 12 h after 25-HCC did not differ and both are shown.

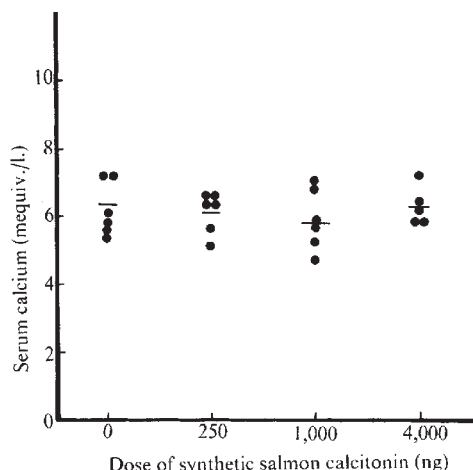


Fig. 4 Serum calcium values. Each point represents one rat. The values at 8 and 12 h after 25-HCC did not differ and both are shown.

producing osteomalacia from this cause during long-term treatment.

This work was supported by grants from the Medical Research Council and the Wellcome Trust. The synthetic salmon calcitonin was a gift from Dr St Guttman of Sandoz Limited, Pharmaceutical Division, Basle, Switzerland. We thank Dr W. F. J. Cuthbertson and Mr T. R. Middleton for help and advice with D-deficient diets.

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Received June 13, 1972.

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- ¹ Blunt, J. W., DeLuca, H. F., and Schnoes, H. K., *Biochemistry*, **7**, 3317 (1968).
- ² Fraser, D. R., and Kodicek, E., *Nature*, **228**, 764 (1970).
- ³ Myrtle, J. F., and Norman, A. W., *Science*, **171**, 79 (1971).
- ⁴ Haussler, M. R., Boyce, D. W., Littledike, E. T., and Rasmussen, H., *Proc. US Nat. Acad. Sci.*, **68**, 177 (1971).
- ⁵ Boyle, I. T., Gray, R. W., and DeLuca, H. F., *Proc. US Nat. Acad. Sci.*, **68**, 2131 (1971).
- ⁶ Galante, L., MacAuley, S. J., Colston, K. W., and MacIntyre, I., *Lancet*, **i**, 985 (1972).
- ⁷ *Lancet*, **i**, 1000 (1972).
- ⁸ Woodhouse, N. J. Y., Reiner, M., Bordier, Ph. J., Kalu, D. N., Fisher, M., Foster, G. V., Joplin, G. F., and MacIntyre, I., *Lancet*, **i**, 1139 (1971).
- ⁹ MacIntyre, I., in *Proceedings of the Calcitonin Symposium (1969)* (edit. by Taylor, S.), **1** (Heinemann, London, 1970).
- ¹⁰ Rasmussen, H., *Clin. Endocr. Metab.*, **1**, 3 (1972).
- ¹¹ Smith, R., Russell, R. G. G., and Bishop, M., *Lancet*, **i**, 945 (1971).
- ¹² Bordier, Ph. J., and Tun Chot, S., *Clin. Endocr. Metab.*, **1**, 197 (1972).
- ¹³ Hill, L. F., Mawer, E. B., Lumb, G. A., and Stanbury, S. W., *Clin. Sci.*, **42**, 16 (1972).

Prevention of Cholera-induced Intestinal Secretion in the Cat by Aspirin

BENNETT¹ has suggested that cholera toxin stimulates the release or synthesis of prostaglandins (PG) which, in turn, interact with the cyclic 3',5'-adenosine monophosphate system to produce diarrhoea. PGs might also be involved in the diarrhoea associated with medullary carcinoma of the thyroid, the carcinoid syndrome and ganglioneuroma²⁻⁴. Diarrhoea

has also been observed in patients with pheochromocytoma (unpublished results of R. L. K.) and large amounts of PGE₂ and PGF_{2α} have been reported in pheochromocytoma⁵. Vane⁶, Smith and Willis⁷, and Ferreira *et al.*⁷ showed that aspirin inhibits the synthesis of PGs in several *in vitro* systems. Bennett¹ therefore suggested that aspirin might prevent the diarrhoea associated with cholera. Our study was undertaken to investigate this possibility in cats.

Cats of either sex weighing 2-4 kg were anaesthetized with sodium pentobarbitone (36 mg/kg) intraperitoneally, and the trachea, femoral artery and vein were cannulated. The animals were artificially ventilated with a Frumin-Lee respirator and inhaled 70% nitrous oxide and 30% oxygen. Femoral arterial pressure was measured with a Statham pressure transducer and recorded on a Beckman-Offner dynograph. Body temperature was maintained at approximately 37°C by an infrared lamp.

The cholera model was a modification of that used by Pierce *et al.*⁸ in the dog. A midline incision was made and the loop of small intestine, from approximately 10 cm distal to the ligament of Treitz to 10-15 cm proximal to the ileocaecal junction, was isolated, keeping the blood supply intact. Both ends of the loop were cannulated with Foley catheters and the balloons were inflated with 2-3 ml. of air. The loop was then flushed with 50 ml. saline followed by 100 ml. air. The abdominal wound was closed and the loop was perfused at a rate of 2 ml./min with a fluid which contained in meq/l. Na⁺ 140, K⁺ 10, Cl⁻ 125, HCO₃⁻ 25, and which had been equilibrated with 5% CO₂ in O₂. The pH of the fluid was 7.58 and its temperature was 37°C as it entered the proximal end of the loop. The fluid drained from the distal Foley catheter by gravity. Every 30 min the loop was gently flushed with 50 ml. air and the volume of effluent was measured. After three 30 min periods (equal to one 90 min collection period) the loop was gently flushed with 100 ml. air and a new 90 min collection period begun. At least one 90 min control period preceded each experiment.

Three series of experiments were carried out. In the control series (ten cats), the loop was perfused for one 90 min collection period, and then 30 ml. of distilled water was injected into the lumen of the loop and retained for 60 min by clamping the catheters. After gently flushing the loop with 100 ml. air, perfusion was resumed and the effluent collected for at least three consecutive 90 min periods. In the second series (six cats), 1.0 g of cholera toxin in 30 ml. distilled water was placed in the loop for 60 min. In the third series (seven cats), toxin was placed in the loop, and 30-60 s later a dose of 25 mg/kg of aspirin ('Aspegic', lot No. 0110501, EGIC Laboratory, France) was injected into the femoral vein. At the end of the experiment the adequacy of the blood supply to the loop was assessed visually. The animal was killed with an intravenous injection of air and the length of the loop measured.

The dose of aspirin chosen was similar to that used in patients with rheumatoid arthritis. Preliminary studies showed that respiratory stimulation always occurred with doses of 100 mg/kg, sometimes with 50 mg/kg, but never with 25 mg/kg. We also found that fluid output after the intravenous administration of aspirin alone was the same as control values.

The volume of effluent collected in the first 90 min perfusion period served as the baseline value against which all subsequent collection periods were compared in a given animal. In the controls (no toxin, no aspirin), the second, third and fourth collection volumes were 104%, 107% and 97% of the initial collection volume of 153 ± 3 ml. s.e.m. In the series with toxin, the second, third and fourth collection volumes were 124%, 135% and 133% of the initial collection volume of 142 ± 8 ml. When toxin and aspirin were given, the second, third and fourth collection volumes were 103%, 109% and 110% of the initial collection volume of 165 ± 5 ml. (Fig. 1). There was no statistically significant difference in fluid output between the control and cholera toxin plus aspirin groups. There was a statistically significant difference in fluid output between the cholera toxin group and the group receiving cholera toxin plus aspirin ($P > 0.01$ at 90, 180 and 270 min).

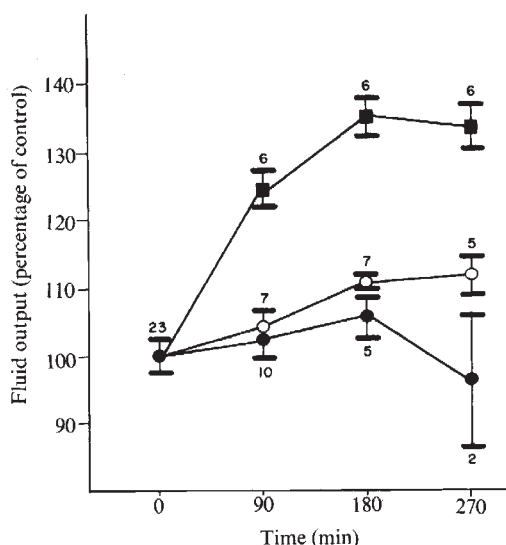


Fig. 1 Prevention of cholera-induced intestinal secretion by aspirin. The zero time figure represents the fluid output over a 90 min control period prior to the intraluminal instillation of either distilled water or cholera toxin in distilled water. The 90, 180 and 270 min values represent the subsequent consecutive 90 min collection periods following removal of the distilled water or cholera toxin from the intestinal loop. Values are means $\pm \frac{s.e.}{mean} \times 100$. ●, Control; ■, cholera toxin; ○, cholera toxin + aspirin.

The similarity of effects produced by cholera toxin and certain PGs has been demonstrated by a number of workers. Greenough *et al.*⁹, studying isolated rabbit ileal mucosal segments, found that the fluids produced in response to cholera toxin, PGA_1 and PGE_1 were of identical electrolyte composition. They suggested^{8,9} that the effects of toxin and PGs might be mediated by cyclic 3',5'-adenosine monophosphate (cAMP), since similar responses were produced by theophylline, which increases levels of cAMP by inhibiting the breakdown by cyclic nucleotide phosphodiesterase. Direct evidence for the involvement of cAMP is that toxin and PGs stimulated adenyl cyclase and increase cAMP levels in a variety of animal tissues¹⁰⁻¹². Furthermore, Chen¹⁴ noted increased levels of cAMP in intestinal biopsy specimens from patients with cholera.

Bennett¹, commenting on these relationships, suggested that aspirin might be of value in the treatment of cholera owing to its inhibition of PG synthesis. This study clearly demonstrates that aspirin inhibits the effects of cholera on fluid secretion in the cat intestine, which agrees with the findings by Jacoby and Marshall in the rat¹⁵.

Despite these experiments, the role of PGs in cholera is not yet clear. Kimberg *et al.*¹³ felt that PGs were not mediators of the cholera toxin response as, after maximal stimulation with PGE_1 , the toxin produced a further increase in cAMP levels. They therefore proposed that similar effects produced by toxin and PG were mediated by different receptors. A different PG or a combination of PGs, which are more potent than PGE_1 , might, however, be involved. Pierce *et al.*⁸ presented other differences between PGs and toxin. The onset of action of PGs was much more rapid than that of the toxin, the former requiring minutes for peak effect, the latter requiring hours. In addition, PGs are most effective when applied to the serosal surface, whereas the toxin is effective when applied to the mucosal surface but not the serosal surface. Furthermore, Sharp and Hynie¹² found that the response to PGE_2 was increased by low doses of toxin, but not by high doses. On the other hand, the similarity of effects of the toxin and PGs on cAMP levels and fluid output and composition led Bennett¹ to suggest mediation of the effects of the toxin by PG. Our observation that aspirin inhibited the effects of the toxin is consistent with this hypothesis. There are, however, alternative explanations of our results: aspirin might inhibit adenyl cyclase,

stimulate phosphodiesterase, or have a nonselective effect in addition to its inhibition of PG synthesis; these possible actions do not seem to have been investigated. Other approaches to determining a role for PGs in cholera would be to study the effects of a variety of PG antagonists in experimental cholera, or to measure the effects of the toxin on PG levels in intestinal tissue.

Regardless of the mechanism by which aspirin antagonizes the effects of cholera, we strongly support Bennett's plea¹ for clinical trials of aspirin. We also suggest that aspirin be tried in the treatment of diarrhoea associated with medullary carcinoma of the thyroid, carcinoid syndrome and bacterial diarrhoea. The cholera toxin (Merck, lot No. 4493G) was supplied by Dr John Seal, National Institute for Allergy and Infectious Diseases, Bethesda.

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- ¹ Bennett, A., *Nature*, **231**, 536 (1971).
- ² Sandler, M., Karim, S. M. M., and Williams, E. D., *Lancet*, ii, 1053 (1968).
- ³ Williams, E. D., Karim, S. M. M., and Sandler, M., *Lancet*, i, 22 (1968).
- ⁴ Bernier, J. J., Rambaud, J. C., Cattani, D., and Prost, A., *Gut*, **9**, 726 (1968).
- ⁵ Vane, J. R., *Nature New Biology*, **231**, 232 (1971).
- ⁶ Smith, J. B., and Willis, A. L., *Nature New Biology*, **231**, 235 (1971).
- ⁷ Ferreira, S. H., Moncada, S., and Vane, J. R., *Nature New Biology*, **231**, 237 (1971).
- ⁸ Pierce, N. F., Carpenter, C. C. J., Elliott, H. L., and Greenough, W. B. III, *Gastroenterology*, **60**, 22 (1971).
- ⁹ Greenough, W. B. III, Pierce, N. F., Al Awqati, Q., and Carpenter, C. C. J., *J. Clin. Invest.*, **48**, 32a (1969).
- ¹⁰ Butcher, R. W., and Baird, C. E., *J. Biol. Chem.*, **243**, 1713 (1968).
- ¹¹ Schafer, D. E., Lust, W. D., Sircar, B., and Goldberg, N. D., *Proc. US Nat. Acad. Sci.*, **67**, 851 (1970).
- ¹² Sharp, G. W. G., and Hynie, S., *Nature*, **229**, 266 (1971).
- ¹³ Kimberg, D. V., Field, M., Johnson, J., Henderson, A., and Gershon, E., *J. Clin. Invest.*, **50**, 1218 (1971).
- ¹⁴ Chen, L. C., Rohde, J. E., Sharp, G. W. G., *Lancet*, i, 939 (1971).
- ¹⁵ Jacoby, H. I., and Marshall, C. H., *Nature*, **235**, 163 (1972).

Moult-inducing Hormones of the Prothoracic Gland of Insects

THE prothoracic gland of insects produces a hormone necessary for moulting to take place¹⁻³, and a steroid hormone called ecdysone has been isolated from whole extracts of silk moth pupae (*Bombyx mori*) that brings about moulting in *Calliphora* larvae deprived of ring glands (containing the prothoracic gland). Similar compounds with moulting-inducing properties have been found in whole extracts of a few insects and in numerous plants⁴, but the presence of this hormone in the prothoracic gland has not been demonstrated.

Nymphs of locusts, such as *Schistocerca gregaria*, have a pair of relatively large prothoracic glands that are easily dissected from the body. Using the isolated locust abdomen bioassay for moulting effect, described by Carlisle and Ellis (unpublished results), we have found that when glands from nymphs in the eighth to eleventh day of the fifth instar (at least 24 h before the next ecdysis) are homogenized in water, centrifuged and the supernatant injected into test abdomens, high positive scores are obtained in the moulting test. Extracts from the glands of one nymph produced 85% positive, while controls produced only 20% positive results.

It is possible to distinguish between substances causing apolysis (separation of cuticle from the underlying epidermis) and others which also stimulate formation of new cuticle by

lifting the cuticle on the dorsal part of the abdomen, and the effect can be confirmed by histological examination. Pure 20-hydroxyecdysone at a dose of 1 μg produced a score of 100% positive in the moulting test with 90% of abdomens showing new cuticle formation; at 10 ng the result was 40% positive, with one quarter of these having new cuticle; 90% of the control group were negative, and the 10% positive, as in the former control group, showed only apolysis.

For the partial purification of moult-inducing substances, the prothoracic glands of 200 late fifth instar nymphs of *S. gregaria* were extracted with distilled water. The extract was centrifuged and the supernatant freeze-dried. The freeze-dried extract (2–3 mg) was partitioned between distilled water (7 ml.) and n-butanol (5 ml.). The aqueous phase was washed in n-butanol (3 ml. and 2 $\times$ 1 ml.). The aqueous fraction gave, on evaporation, a residue (0.8–1 mg) which was inactive when tested at levels of 200, 100 and 60 μg per abdomen in the locust abdomen test. The butanol fraction (0.7–1 mg) was chromatographed on thin layer plates (5 $\times$ 20 cm) coated with silica gel (0.25 mm layer of 'Kieselgel' PF₂₄₅, Merck, Darmstadt) which had been deactivated by storing over saturated sodium chloride solution. The chromatogram was developed in chloroform–95% ethanol (4:1 v/v). The silica gel was removed from the plate in bands and the material eluted with methanol. The moulting activity of the materials obtained is shown in Fig. 1. The substances from the two bands of activity caused apolysis but not formation of new cuticle.

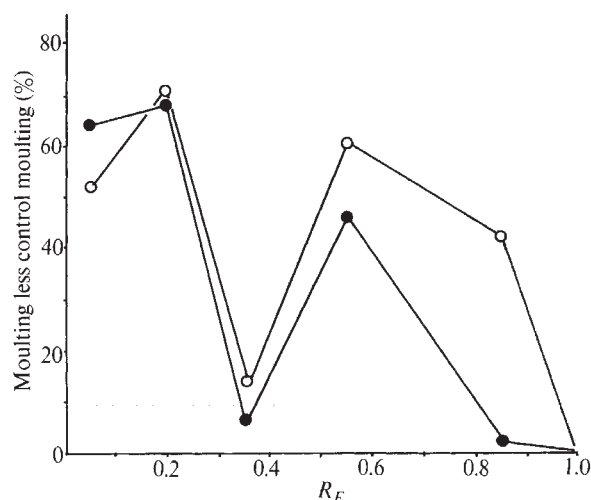


Fig. 1 Variation of moulting activity, determined by locust abdomen bioassay, with R_F of extract of prothoracic glands of late fifth instar *S. gregaria*, on thin layer chromatography. Samples were recovered from chromatograms and dissolved in 400 μl . distilled water and assayed at 20 μl . per abdomen (○); portions were diluted 5 times and again assayed at 20 μl . per abdomen (●). Glands extracted with water.

Similarly, methanol extracts of whole bodies of late fifth instar *S. gregaria*, purified 1,000-fold by solvent partition and chromatography, were subjected to preparative layer chromatography (on 20 cm $\times$ 40 cm $\times$ 2.5 mm layers), and gave a double peak of activity (Fig. 2) of a pattern similar to that obtained with glands. The material from the band of low R_F from whole nymphs showed high activity in apolysis and moderate activity in formation of new cuticle, but this was further resolved into two active fractions, one of which induces apolysis, and another which causes formation of new cuticle and which has been shown by gas chromatography and mass spectrometry to be 20-hydroxyecdysone⁶.

The fresh weight of the two prothoracic glands in a fifth instar locust represents 10^{-4} times the weight of the whole insect. From a comparison of the number of glands and whole nymphs required to produce similar levels of activity in the bio-

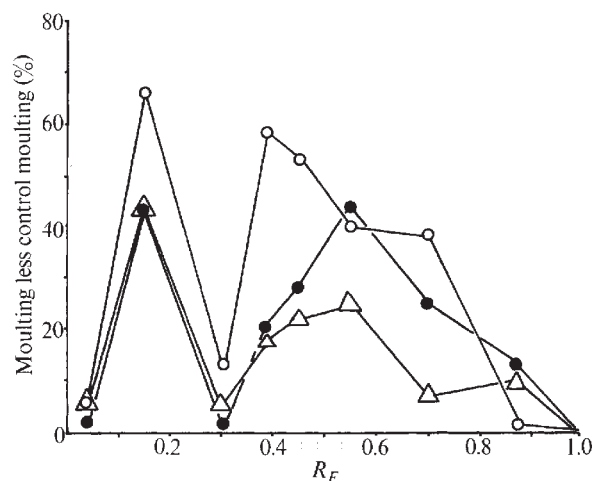


Fig. 2 Variation of moulting activity, determined by locust abdomen bioassay, with R_F on P.L.C. plates, on 240 mg of active extract of whole bodies of fifth instar *S. gregaria*. Samples were recovered from chromatograms, and portions dissolved in distilled water and assayed at three concentrations: (○) 100 μg per abdomen, (●) 10 μg per abdomen and (Δ) 1 μg per abdomen.

assay, the concentration of the two substances found in the glands must be about 100 times greater in the prothoracic gland than in the whole tissues.

Gas chromatographic determination of the amount of ecdysone and 20-hydroxyecdysone in prothoracic glands and whole nymphs on each day of the fifth instar was carried out by the method of Morgan and Woodbridge⁶. 20-Hydroxyecdysone, but not ecdysone, was detected in varying amounts (12–270 ng per insect) throughout the instar in whole locusts. Neither hormone was detected in prothoracic glands. At the time of maximum 20-hydroxyecdysone titre, 5 ng of ecdysone would have been detected in whole body extracts, and as little as 2% of the total ecdysones present in whole bodies would have been detected in prothoracic glands. Because of the small size of the gland, this limit could still permit the substance to be 80 times more concentrated in the gland than in the whole body. The amount (less than 2 ng) would be too little, however, to account for the level of activity found in the gland, and for the kind of activity, which did not induce new cuticle formation as did 20-hydroxyecdysone isolated from whole nymphs.

Of three substances with moulting effect found in the desert locust, 20-hydroxyecdysone could not be detected in the prothoracic gland. The other two are present in greater concentrations in the glands than in whole tissues. These latter substances produce apolysis and early stages of moulting in test abdomens, and this effect is different from that of 20-hydroxyecdysone which stimulates new cuticle formation.

We suggest that the prothoracic gland does not itself produce 20-hydroxyecdysone, but instead produces another hormone, or hormones, which trigger(s) the formation of 20-hydroxyecdysone formation in another part of the body⁷. From the work of Weir⁸, Locke⁹ and Romer¹⁰, this site may well be the oenocytes of the abdomen, which, in the locust, spread to form a sheet beneath the epidermal cells during the latter part of the instar.

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¹ Fukuda, S., *J. Fac. Sci. Tokyo Univ.*, **6**, 477 (1944).

² Williams, C. M., *Biol. Bull., Woods Hole*, **90**, 234 (1947).

- ³ Wigglesworth, V. B., *J. Exp. Biol.*, **29**, 561 (1952).
- ⁴ Karlson, P., *Vitamins Hormones*, **14**, 227 (1956).
- ⁵ Horn, D. H. S., *Naturally Occurring Insecticides* (edit. by Jacobson, M., and Crosby, D. G.) (Marcel Dekker, New York, 1971).
- ⁶ Morgan, E. D., and Woodbridge, A. P., *Chem. Commun.*, **1971**, 475 (1971).
- ⁷ Moriyama, H., Nakanishi, K., King, D. S., Okauchi, T., Siddall, J. B., and Hafferl, W., *Gen. Comp. Endocrinol.*, **15**, 80 (1970).
- ⁸ Weir, S. B., *Nature*, **228**, 580 (1970).
- ⁹ Locke, M., *Tissue and Cell*, **1**, 103 (1969).
- ¹⁰ Romer, F., *Naturwissenschaften*, **58**, 324 (1971).

Porphyrin Pigmentation in Deep-sea Medusae

THE photosensitizing effect of some porphyrins prevents their accumulation in the epidermal layers of animals living in well-illuminated environments, unless the porphyrins are accompanied by some other screening pigment or the animal can retreat into a dark micro-environment¹⁻⁴. Thus some shallow water marine annelid worms contain considerable quantities of porphyrins in their tissues, but are tubicolous or burrowing in habit⁵. They are difficult to maintain in the light in the laboratory, often exhibiting symptoms which could be said to resemble those of human porphyria⁶. Beneath the immediate surface layers of the ocean, however, light intensity is rapidly reduced to very low values, and the deep sea is in almost total darkness. Kennedy⁷ has noted that the low light intensities in which many marine animals live would prevent the appearance of porphyria symptoms leading to illness and death in the human subject. In these conditions, the accumulation of porphyrins is no longer hazardous, and they may be used like any other pigment for purposes of tissue coloration. The identification of free porphyrins as the source of the general body coloration of certain deep-sea medusae supports this view.

Specimens of the bathypelagic scyphozoans *Atolla wyvillei* and *Periphylla periphylla* were collected in the eastern north Atlantic during cruises of RRS Discovery in 1970 and 1971, and stored at -20°C for laboratory analysis. Both species have a characteristic purple-brown or red-brown pigmentation, only in the stomach wall and manubrium in the smallest specimens, but extending over most of the body in larger ones. In the fresh animal, the pigment is not appreciably fluorescent in ultraviolet light, although diluted homogenates are slightly red fluorescent. This property is not affected by boiling or by dilute alkali extraction, but treatment with acetone, ethanol and organic and mineral acids causes a brilliant red fluorescence to appear. The tissues of *Atolla* and *Periphylla* were homogenized in ethyl acetate/acetic acid (3:1 v/v) and the extracts washed with sodium acetate solution to remove the acid. The pigments were then extracted with several washes of 5% HCl. The acid extracts were pooled, diethyl ether added, and ether extraction promoted by addition of solid sodium acetate. The ethereal layer was washed with water and dried over anhydrous sodium sulphate. The adsorption spectrum of the pigment had maxima in 2.7 M HCl at 410 nm, 556 nm and 600 nm, and in pyridine at 409 nm, 508 nm, 542 nm, 577 nm and 632 nm, very close to those of protoporphyrin IX in the same solvents. Descending chromatograms ('Whatman' No. 1 paper; 20°C) developed with a solution of 2:6 lutidine in water (5:3.5 v/v) in an atmosphere of ammonia⁸ gave an R_F (0.81) indicative of a dicarboxylic porphyrin, and identical with that of protoporphyrin (Sigma Chemical Co.).

The pigments were more rapidly extracted in the esterified form by methanol containing 5% by volume of concentrated sulphuric acid. After filtration, chloroform was added and then sufficient water to separate the chloroform solution as a reddish purple hypophase with a brilliant red fluorescence. The chloroform was run off, washed several times with sodium acetate solution and water, dried and removed on a rotary

evaporator. The pigment residues were redissolved in dry chloroform and chromatographed first on Grade IV alumina, then on Grade III magnesia^{9,10}. From alumina the pigments from both species were eluted with benzene/chloroform (10:1 v/v) and from magnesia with chloroform/methanol (100:3 v/v). These eluants are indicative of the dimethyl ester of a dicarboxylic porphyrin¹⁰. Both purified pigments had an actio-type absorption spectrum with maxima in chloroform at 409 nm, 507 nm, 542 nm, 577 nm and 632 nm, and a shoulder at 602 nm. Maxima in pyridine were at similar wavelengths, 410 nm, 507 nm, 542 nm, 577.5 nm and 633 nm with a shoulder at 605 nm. In the same solvents protoporphyrin IX dimethyl ester had almost identical absorption spectra with maxima at similar wavelengths (± 1 nm). The esterified pigments were reduced by catalytic hydrogenation over Pd¹¹. The reduction products had absorption spectra with maxima (± 1 nm) in chloroform at 400 nm, 498 nm, 532 nm, 565 nm and 620 nm, very similar to that of mesoporphyrin dimethyl ester. Chromatography of esterified *Atolla* and *Periphylla* pigments with protoporphyrin and mesoporphyrin dimethyl esters on paper chromatograms developed with the first solvent system of Chu and Chu¹² showed that the reduced pigments had the same mobility as esterified mesoporphyrin and were now clearly separable from esterified protoporphyrin. On this evidence the pigments of both *Atolla* and *Periphylla* are identified as free protoporphyrin.

Porphyrin pigmentation has not been found in either of the relatively shallow-living medusae *Pelagia*¹³ and *Aurelia*¹⁴, but the characteristic purple-brown colour of many deep-sea medusae suggests that porphyrin pigmentation is not restricted to the two species so far analysed. MacMunn¹⁵ identified the 'polyperrythrin' extracted by Moseley from the medusan *Cassiopeia* and several deep-water corals as 'haematoporphyrin' (the only porphyrin recognized at that time). The distribution of the pigment suggests that at least one function may be to absorb the light produced by the bioluminescence of prey in the gut. Another may be the prevention of reflexion of ambient daylight or bioluminescence from some of the animals' tissues. At a day depth of only 500 m the ambient light intensity in the *clearest* ocean water is about 10^{-7} that of sunlight (or 10^{-1} that of moonlight)¹⁶ and is virtually monochromatic at about 480 nm. Bioluminescent light is likely to be of even lower intensity and of similar wavelength¹⁶. In these conditions of very low intensity near-monochromatic blue light, the role of melanin in fishes and carotenoids in decapod crustaceans may be played in the medusae by protoporphyrin, without the hazards that would be attendant on its use in high intensity light of a broader spectrum. The form in which the protoporphyrin occurs in the tissues is not yet clear, for though its fluorescence is largely quenched it cannot be extracted with strong buffer solutions as a protein complex. Free porphyrins have not been reported from other bathypelagic invertebrates, but do occur in the photophores both of certain bathypelagic fishes and, possibly, of some squid (P. J. H., unpublished results).

I thank Professor G. Y. Kennedy for criticism of the manuscript.

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Received December 17, 1971; revised April 24, 1972.

- ¹ Fox, H. M., and Vevers, G., *The Nature of Animal Colours* (Sidgwick and Jackson, Ltd, London, 1960).
- ² Delkeskamp, E., *Zeit. Vergl. Physiol.*, **48**, 400 (1964).
- ³ Kennedy, G. Y., and Vevers, H. G., *J. Marine Biol. Ass. UK*, **32**, 325 (1953).
- ⁴ Kennedy, G. Y., *J. Marine Biol. Ass. UK*, **38**, 27 (1959).
- ⁵ Mangum, C. P., and Dales, R. P., *Comp. Biochem. Physiol.*, **15**, 237 (1965).
- ⁶ Mangum, C. P., cited by Segal, E., *Marine Ecology* (edit. by Kinne, O.), **1**, part 1, 161 (Wiley-Interscience, 1970).

- ⁷ Kennedy, G. Y., *Chemical Zoology* (edit. by Florkin, M., and Scheer, B. T.), 4, 311 (Academic Press, New York and London, 1969).
- ⁸ Falk, J. E., Dresel, E. I. B., Benson, A., and Knight, B. C., *J. Biol. Chem.*, 63, 87 (1956).
- ⁹ Brockmann, A., and Schodder, H., *Chem. Ber.*, 74, 73 (1941).
- ¹⁰ Nicholas, R. E. H., *Biochem. J.*, 48, 309 (1951).
- ¹¹ Muir, H., and Neuberger, A., *Biochem. J.*, 45, 163 (1949).
- ¹² Chu, T. C., and Chu, E. J., *J. Biol. Chem.*, 208, 537 (1954).
- ¹³ Fox, D. L., and Millott, N., *Proc. Roy. Soc., B*, 142, 392 (1954).
- ¹⁴ Czezug, B., *Marine Biology*, 5, 141 (1970).
- ¹⁵ MacMunn, C. A., *J. Physiol.*, 7, 240 (1886).
- ¹⁶ Clarke, G. L., and Denton, E. J., *The Sea* (edit. by Hill, M. N.), 1, 456 (Interscience, New York and London, 1962).

Vitamin C Requirements and Oral Contraceptives

ANIMAL experiments¹⁻⁴ indicate that oestrogens increase the rate of ascorbic acid breakdown and lower tissue levels. Vitamin C is poorly stored by humans and widespread sub-clinical deficiencies occur. We have investigated levels of ascorbic acid in blood cells from healthy women, some of whom were taking oral contraceptives. We have also studied pregnant women and others receiving an injected contraceptive. None was receiving supplementary vitamins.

Several brands of "combined-type" oral contraceptives were in use, while the injected product was 'Depo-Provera' (150 mg medroxyprogesterone acetate every 3 months).

Blood was collected by venepuncture and 3.0 ml. added to a special diluting agent⁵, any remainder being added to plastic tubes containing EDTA. A combined leucocyte-platelet button was prepared from the former, and a relatively pure platelet button from the latter. Ascorbic acid was determined by 2,4-dinitrophenylhydrazine⁵ and expressed as $\mu\text{g}/10^8$ cells for the leucocytes and as mg/g for the platelets. Mean values for each group are set out in Tables 1 and 2. We also measured ascorbic acid in blood cells from small groups of young women before and after beginning treatment with steroid contraceptives, and in others receiving no treatment. These results are shown in Table 3.

85 women took part in the main study; 31 were untreated non-pregnant controls (mean age 27 yr), 18 were pregnant (mean 24 yr), while 39 were receiving steroid contraceptives (mean 27 yr). Each group contained European, African and Asian women. For those in the contraceptive group, 21 had been under treatment for under 6 months, 4 for between 6 and 12 months, and 14 for over 1 year.

Our results show that ascorbic acid in both leucocytes and

Table 1 Leucocyte Ascorbic Acid Content

Group	No.	Ascorbic acid: ($\mu\text{g}/10^8$; mean $\pm$ s.d.)	P value* (t-test)
All controls	31	39 $\pm$ 28	—
African controls	12	40 $\pm$ 24	NS
All contraceptives	39	26 $\pm$ 22	<0.01
Norgestrel products	15	27 $\pm$ 21	<0.02
Ethinodiol diacetate products	6	23 $\pm$ 19	<0.02
Lynestrinol products	4	25 $\pm$ 10	<0.05
Norethisterone acetate products	7	26 $\pm$ 17	<0.02
Other products	3	25 $\pm$ 19	<0.02
Depot contraceptive	4	38 $\pm$ 17	NS
All pregnant	18	34 $\pm$ 21	NS
First trimester	1	19	—
Second trimester	9	33 $\pm$ 23	NS
Third trimester	8	37 $\pm$ 21	NS

* Each group is compared with the complete control group: P values greater than 0.05 are listed as NS (not significant).

Table 2 Platelet Ascorbic Acid Content

Group	No.	Ascorbic acid: (mg/g wet weight) mean $\pm$ s.d.	P value
All controls	10	0.26 $\pm$ 0.11	—
Oral contraceptives*	10	0.19 $\pm$ 0.13	<0.01
Depot contraceptive	5	0.28 $\pm$ 0.14	NS
Pregnant	5	0.24 $\pm$ 0.10	NS

* As the group is small, it has not been subdivided by product: it contained 3 patients taking 'Gynovlar', 5 taking 'Ovral' or 'Eugynon' (equivalent) and 2 taking 'Ovulen' 50.

Table 3 Leucocyte and Platelet Ascorbic Acid before and after Treatment with Oral Contraceptives

Group	Age of subject	Product	Interval (months)	Ascorbic acid			
				Leucocyte		Platelet	
Contra- ceptive	31	'Lyndiol' 2.5	2	38	19	0.30	0.25
	22	'Minilyn'	1	65	38	0.27	0.22
	23	'Depo-Provera'*	1	28	29	0.24	0.26
	35	'Neogynon'	1	29	16	0.19	0.15
	23	'Eugynon'	2	32	28	0.23	0.16
	20	'Ovulen' 50	2	45	32	0.28	0.20
Control	28	None	1	31	34	0.24	0.27
	20	None	1	23	28	0.18	0.20
	19	None	1	28	31	0.26	0.28
	21	None	1	38	32	0.28	0.25
	18	None	1	42	38	0.24	0.19

Ascorbic acid concentrations for leucocytes are $\mu\text{g}/10^8$ cells and for platelets mg/g wet weight. The values shown under column 1 are pre-treatment and under column 2 post-treatment results.

* Injectable contraceptive.

platelets is significantly lower in women taking steroid contraceptives than in untreated controls or in pregnant women. Only the injected contraceptive appeared not to influence the vitamin C concentration. Cell ascorbic acid was also significantly lower in the 5 women studied before and after beginning oral contraceptives, but not in the woman starting 'Depo-Provera', nor in the untreated group.

It seems likely that oral contraceptive steroids increase the breakdown of ascorbic acid, perhaps by their stimulant action on liver release of ceruloplasmin⁶, a copper-containing protein with ascorbate oxidase activity⁷. It seems clear that many women receiving oral contraceptives may be in an induced hypovitaminotic C condition and require supplementary vitamin. It is possible that some of the reported side-effects of "the pill" may be a consequence of this vitamin lack.

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- ¹ di Martini, Marrubini, G., and Silo, N., *Arch. Fisiol.*, 50, 94 (1950).
- ² Mosonyi, J., *Hoppe-Seyler's Z. Physiol.*, 242, 158 (1936).
- ³ Clemetson, C. A. B., *Lancet*, ii, 1037 (1968).
- ⁴ Saroja, N., Mallikarjuneswara, V. R., and Clemetson, C. A. B., *Contraception*, 3, 269 (1971).
- ⁵ Denson, K. W., and Bowers, E. F., *Clin. Soc.*, 21, 157 (1961).
- ⁶ Russ, E. M., and Raymunt, J., *Proc. Soc. Exp. Biol. Med.*, 92, 465 (1956).
- ⁷ Osaki, S., McDermott, J. A., and Frieden, E., *J. Biol. Chem.*, 239, 3570 (1964).

Hyperbaric Oxygen: an Adjuvant in Renal Preservation

HYPERBARIC oxygen retards metabolic processes¹ and also increases the volume of oxygen in solution; this phenomenon is enhanced by the increased solubility of oxygen at low temperatures.

These apparently desirable effects of high pressure oxygen aroused interest in its possible role as an adjuvant to hypothermia in organ preservation. It has not always been possible, however, to demonstrate convincing enhancement of preservation when hyperbaric oxygen has been used in conjunction with simple surface cooling or surface cooling after the kidney has been flushed out with a chilled solution²⁻⁴.

Hypothermic perfusion at low flow rates in hyperbaric conditions has allowed successful preservation of the canine kidney for 24 h⁵, and modifications of this technique have resulted in extension of the period of preservation to 72 h⁶.

We performed three groups of experiments to examine the effect of trickle perfusion and hyperbaric oxygen on renal preservation, using mongrel dogs. Anaesthesia was induced with thiopentone and maintained with an oxygen, nitrous oxide and halothane mixture administered through an endotracheal tube. The animals were given 1 l. of Hartman's solution and 7.5 g mannitol intravenously during the operation to remove the kidney, and on reimplantation they received the same quantity of mannitol and 1.5 l. of Hartman's solution. The right kidney was removed and flushed for 5 min with a chilled solution (modified Collins C4 solution⁷) (Table 1). The kidneys were then maintained at 5° C for 24 h and reimplanted into the iliac fossa after the contralateral kidney had been removed.

Table 1 Perfusate Composition

Quantities per litre	
KH ₂ PO ₄	2.05 g
K ₂ HPO ₄	7.40 g
KCl	1.12 g
NaHCO ₃	0.84 g
'Dextran' 40	50 g
Dextrose	25 g
Procaine HCl	100 mg
Chlorpromazine	16 mg
Phenoxybenzamine	25 mg
Heparin	5,000 µg
Osmolarity adjusted to 320±5 with glucose pH at 20° C	7.4

In Group 1 the kidneys were immersed in the cold perfusate after flushing and stored at ambient pressure, but in Group 2 the kidneys were perfused at ambient pressure for 4 h in a 'Vickers THS/4' unit at a rate of 2 ml./min, after which the perfusion was discontinued: the perfusate was oxygenated throughout the period of perfusion. Group 3 differed from Group 2 only in that the entire preservation after flushing was conducted under 4 atm. abs. oxygen.

The results are shown in Table 2. In Group 1 two out of six animals survived. One dog which was killed as a result of an injury nine days postoperatively was considered to have had a successful preservation as the serum creatinine had fallen from a peak of 10.8 to 7.4 mg/100 ml. by the time of the accident. In Group 2 three out of six animals survived, and three died of uraemia. In Group 3 all six animals survived. The difference between the proportions surviving in Groups 2 and 3 is statistically significant (difference = 2 × s.e.; *P* = 0.05).

Hyperbaric oxygen probably enhances preservation of tissues by retardation of metabolic processes. It is not clear precisely how this occurs, but it is known that certain enzyme systems are inhibited⁷⁻¹⁰, and that hyperbaric oxygen interferes with the electron transfer chain¹¹. Kidneys have been preserved for 24 h under hyperbaric helium and nitrogen¹², suggesting that pressure *per se* may be important, but hyperbaria would appear

Table 2 Quantities of Serum Creatinine in Three Test Groups

		Serum creatinine (mg/100 ml.)							
		Day							
		-1	0	1	3	7	14	21	28
Group 1	Dog								
	Q	1.1	1.3	4.5	10.7*				
	W	1.0	1.5	4.8	11.8	20.4*			
	Ii	1.0	1.0	5.0	7.8	10.8*			
	T	1.0	1.6	4.6	9.7	10.8†			
	R	1.1	1.3	5.3	7.9	4.1	1.7	1.4	1.2
Group 2	Dd	1.0	1.1	2.0	2.8	1.3	1.3	1.0	1.0
	Aa	0.9	1.2	4.4	9.8*				
	Z	1.1	1.2	4.4	8.8	15.4*			
	Kk	1.0	1.6	6.2	19.8	19.0*			
	X	1.1	1.6	3.5	5.7	4.6	1.6	1.6	1.5
	Cc	0.9	0.9	4.8	8.9	6.4	3.5	1.4	1.4
Group 3	B	1.1	1.6	3.7	8.4	9.1	1.8	1.4	1.4
	S	1.0	1.3	3.9	5.5	3.6	2.1	1.5	1.7
	Oo	0.9	1.5	3.4	4.2	2.5	1.8	1.9	1.5
	U	1.2	1.5	4.1	7.1	3.8	2.9	1.6	1.5
	O	0.9	1.4	3.6	6.0	2.9	1.2	1.2	1.5
	Bb	1.0	1.2	2.8	3.0	2.2	1.8	1.5	1.2
	M	0.9	1.1	2.8	2.5	2.0	1.3	1.2	1.2

* Died of uraemia.

† Injured and therefore killed.

not to inhibit metabolism *in vivo* as men have lived for 22 days under 12 atm. abs.¹³.

Calne *et al.*¹⁴ suggested that trickle perfusion would merit investigation for organ preservation, but, on the basis of these experiments, we feel that trickle perfusion alone offers no advantage over a simple flushing of the kidney, although trickle perfusion under hyperbaric oxygen results in improved preservation.

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¹ Bert, P., *La Pression Barometrique* (Paris, 1878).

² Manax, W. G., Bloch, J. H., Longerbeam, J. K., and Lillehei, R. C., *Surgery*, **56**, 275 (1964).

³ Basso, M. D., Calne, R. Y., and Hopkinson, W. I., *Brit. J. Urol.*, **39**, 276 (1967).

⁴ Collins, G. M., Bravo-Shugarman, M., and Terasaki, P. I., *Lancet*, **ii**, 1219 (1969).

⁵ Ackermann, J. R. W., and Barnard, C. N., *Brit. J. Surg.*, **53**, 525 (1966).

⁶ Snell, M. E., and Hopkinson, W. I., *Surgical Research Society* (London, January 1972).

⁷ Haugaard, N., *Ann. New York Acad. Sci.*, **117**, 736 (1965).

⁸ Wood, J. D., and Watson, W. J., *Canad. J. Physiol. Pharmacol.*, **4**, 27 (1964).

⁹ Hall, I. M., and Sanders, A. P., *Proc. Exp. Biol. Med.*, **121**, 1203 (1966).

¹⁰ Thomas, jun., J. J., Neptune, E. M., and Sudduth, H. C., *Biochem. J.*, **88**, 31 (1963).

¹¹ Chance, B., Jamieson, D., and Coles, H., *Nature*, **206**, 257 (1965).

¹² Lyons, G. W., Dietzman, R. H., and Lillehei, R. C., *Trans. Amer. Soc. Artif. Int. Organs*, **12**, 236 (1966).

¹³ Cousteau, J.-Y., *National Geographic*, **129**, 498 (1966).

¹⁴ Calne, R. Y., Dunn, D. C., Gajo-Reyer, R., Hadjiyannakis, E. J., and Robson, A. J., *Nature*, **235**, 171 (1972).

High Altitude, Haematocrit and Age

ALTHOUGH the relationship between haematocrit and altitude was established by Hurtado *et al.*¹ in the Andes of Peru, none has been established between haematocrit and the age of permanent residents at different altitudes. Reviewing data collected from healthy volunteers living in Morococha, 4,540 m

above sea level, we found that there was always a pronounced increase in haematocrit with age, which was surprising because of the short time between surveys. We have made haematocrit determinations with the help of healthy male subjects, aged 4 to 46 y, in Morococha, Cerro de Pasco (4,250 m above sea level) and Puno (3,800 m above sea level).

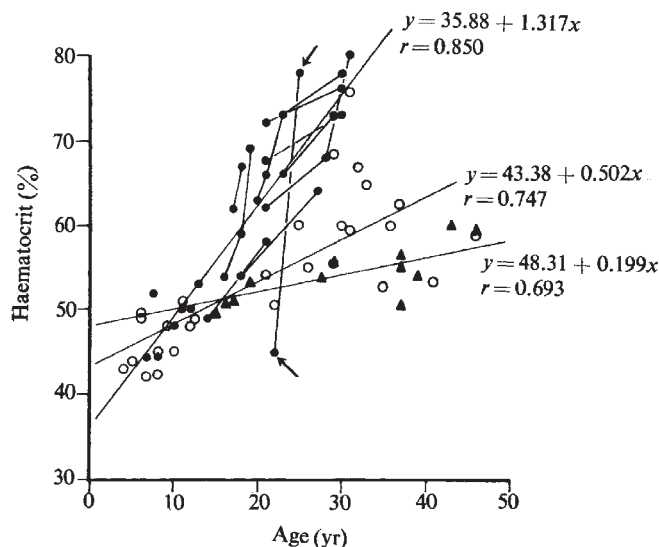


Fig. 1 Mass plot of haematocrits as a function of age. ●, Morococha 4,500 m; ○, Cerro de Pasco 4,200 m; ▲, Puno 3,800 m.

Fig. 1 shows a mass plot of haematocrits as a function of age. Apart from individual determinations, it shows the linear regression lines corresponding to the three altitudes studied. The slopes vary markedly. A *t* test showed significant difference; <0.01 between Puno and Cerro de Pasco, and <0.001 between Cerro de Pasco and Morococha. It is interesting that the three lines intersect in a narrow triangular zone, indicating a tendency to a more uniform haematocrit below the age of 15. Fig. 1 also shows lines joining individual values for the Morococha group, demonstrating the progression of haematocrits with age. The individual trend follows that of the regression line. Wintrobe², reviewing the literature on haematocrits and age at sea level, described an increase in haematocrits from approximately one year old to about 18; thereafter, the haematocrit remains constant to beyond the age of 63. Our high altitude groups are markedly different from Wintrobe's sea level group, in that the haematocrit increases continuously from childhood onwards. Fig. 1 shows that in Morococha a haematocrit of about 75% is predictable at age 30. That level would be reached in Cerro de Pasco at about 63, according to the extrapolation of our regression equation.

We consider these observations to be pertinent to the public health of the inhabitants of the Andean area, where 40 million people live above 2,000 m. Loss of the capacity to live at high altitudes, usually accompanied by excessive polycythaemia, has been called chronic mountain sickness, or Monge's disease^{3,4}. A haematocrit of 75% is often accompanied by symptoms of chronic mountain sickness, which the natives of Morococha have learned to alleviate temporarily by frequent bleedings carried out at small infirmaries, or by migrating to a lower altitude at periodic intervals. In Fig. 1, the arrows point to values obtained in a subject who was bled and then showed a rapid increase in haematocrit. Although we have shown that 24 h after bleeding, the pO_2 , pCO_2 and pH of the arterial blood are not significantly changed⁵, recent studies in Peru prove that bleeding does produce a significant increase in SO_2 after 5 days⁶. With the rapid increase in

population in the Andean area, which has been shown to be faster than at sea level⁷, chronic mountain sickness is expected to increase in incidence if migration to lower altitudes does not accelerate.

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- ¹ Hurtado, A., Merino, C., and Delgado, E., *Arch. Int. Med.*, **75**, 284 (1945).
- ² Wintrobe, M. M., *Clinical Haematology* (Lea and Febiger, Philadelphia, 1962).
- ³ Monge, M. C., *Arch. Int. Med.*, **59**, 32 (1937).
- ⁴ Monge, M. C., *Science*, **95**, 79 (1942).
- ⁵ Monge, C. C., Lozano, R., and Whittembury, J., *Nature*, **207**, 770 (1965).
- ⁶ Sime, F., unpublished observations, 1971, cited in Ciba Foundation Symposium on *High-Altitude Physiology: Cardiac and Respiratory Aspects*, 53 (1971).
- ⁷ Monge, M. C., and Monge, C. C., *High-Altitude Diseases* (Thomas, Springfield, Illinois, 1966).

Control of the Heart Rate by External Stimuli

THE human cardiac pacemaker behaves as a nonlinear oscillator, whose period can be varied over a certain range by sympathetic and parasympathetic control. We have been able to vary the heart rate of human subjects non-invasively by causing an entrainment of the sinus rhythm with external auditory stimuli. This presumably acts through the nervous control mechanisms, and results from a neural coupling into the cardiac centres of the brain. It represents, therefore, a new adjunct to the "instrumental learning" control of autonomic activity, and, unlike the latter, does not require the determined effort of the subject.

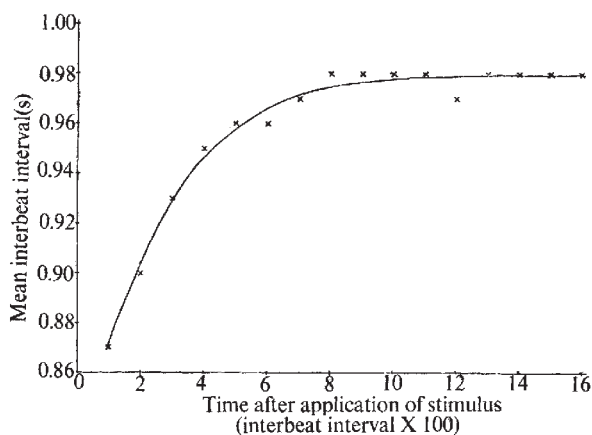


Fig. 1 Plot of the interbeat interval (averaged over 200 intervals) after application of the audible stimulus. The final level was maintained for the duration of the stimulus sequence.

Our method is to generate an audible click in a loudspeaker at a precise time in the cardiac cycle measured from each R-wave of the subject's ECG. If this stimulus does not fall within a certain restricted time range, which depends on the particular subject, and is apparently less than 0.1 s, no control can occur and the heart rate does not alter. If, however, it does fall within the critical range, the heart rate can be caused to increase or

decrease with a time constant of several minutes. The new rate is maintained until the stimulus is removed, when it reverts to its previous value.

Fig. 1 shows the course of the mean interbeat interval in a typical case after application of the stimulus. It is plotted as the mean interval over 200 beats, with the average moved 100 beats at a time. The mean interval changed more or less exponentially from 0.87 s to 0.98 s, an increase of about 12%, with a time constant of about 3 min.

Fluctuations in interbeat intervals caused (primarily) by breathing still occur, of course, but these tend to be less when the heart is entrained in this way. In the case already given, the standard deviation of intervals was 0.08 s before application of the stimulus, and 0.05 s after the new level had been reached.

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Received February 7, 1972.

Telemetry of Heart Rate in Diving Seals

THE changes in heart rate during dives by seals have hitherto been recorded mainly from animals restrained in various ways and forcibly submerged at sea and in tanks¹⁻⁴ for periods determined by the investigator and not by the seal. Heart rate recordings have also been made from seals free-swimming but in a harness with trailing ECG leads from cutaneous axillary electrodes³. The diving bradycardia is probably less profound in seals diving quite unrestrained⁴.

Radiotelemetry devices⁵ have been implanted in the hypodermis of the back and neck of 12-18 month old grey seals (*Halichoerus grypus*) to follow heart rate changes in unrestrained seals trained to dive on command. The package had electrodes extending through the hypodermis across the thorax and the ECG could be broadcast continuously over a period of several months: a magnetic switch turned the transmitter on and off. This made possible prolonged experiments on ECG characteristics and changes in cardiac rhythm in relation to respiratory rhythm on land, during sleep and during diving in unrestrained seals and to compare them with findings in restrained seals. Similar dives were carried out with seals containing transmitters but with the animals forcibly submerged in a cage lowered into a tank.

The seals were trained to submerge on command signalled by an underwater light. When the light was turned off and a whistle sounded as a bridging stimulus a fish was delivered by an underwater feeder. Thus the seals could be instructed to make voluntary dives of periods of submersion up to eight minutes and recordings were made before, during and after the dive.

Out of water respiratory rate was 2-12 min⁻¹, the heart rate was 120-150 beats min⁻¹ but fell to 40-70 during the breath holds which occurred regularly for 20-50 s at intervals of 30 s per min. Asleep, out of water, the respiratory rate was 8-15 and the heart rate was 140-170.

The resting respiratory rate in water was 3-5 and heart rate was 110-170; this fell to 33-48 during the short breath hold periods. During forced restrained dives the heart rate fell to as low as 10-40 beats min⁻¹. During trained dives the heart rate fell to 20-40 but in these young grey seals there was often a continual fluctuation in the bradycardia. A seal would sometimes, but not always, exhale under water between 0.25-1.0 l. air once or several times during a trained dive of 2-8 min. On these exhalations the heart rate rose from about

30 to 65-100 for a few seconds. When the whistle was sounded as a bridging stimulus and the seal took and ate its fish under water the heart rate increased from about 30 to 60-80 for a few seconds, followed by a sharp fall in heart rate for a further few seconds while the seal returned to the surface. The heart rate then immediately rose to 150-180.

Seals submerged in a glass observation tank completely filled with water but with a small breathing hole were seen to exhale under water a large bubble of air (250-750 ml.) which remained beneath the surface glass sheet. On exhaling, the seal's heart rate rose momentarily as during other exhalations under water. The seal would dive to the bottom of the tank but after 30-60 s it returned to the bubble of exhaled air still beneath the glass and inhaled it almost entirely with again a momentary increase of heart rate. Such behaviour might be of value to seals making prolonged shallow dives under ice, since carbon dioxide would rapidly diffuse from the air bubble into the seawater. It is known that Weddell seals can swim under ice for 2,000-4,400 m from one breathing hole to the next and remain submerged for more than 1 h⁶.

We suggest that during forced and restrained dives there is a maximum dive response as judged by bradycardiac characteristics. The bradycardia is less marked during trained dives and there are momentary periods of partial release associated with intrathoracic adjustments. To what extent these changes in heart rate are facultative is difficult to assess but at least in any forced dive the degree of response suggests that the seal is preparing for an extended period of immersion.

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Received April 24, 1972.

¹ Scholander, P. F., *Hyalrad. Skr.*, **22**, 1 (1940).

² Harrison, R. J., *Nature*, **188**, 1068 (1960).

³ Harrison, R. J., and Tomlinson, J. D. W., *Viewpoints in Biology* (edit. by Carthy, J. D., and Duddington, C. L.), **2**, 115 (Butterworths, London, 1963).

⁴ Harrison, R. J., and Kooyman, G. L., in *The Behavior and Physiology of Pinnipeds* (edit. by Harrison, R. J., Hubbard, R. C., Peterson, R. S., Rice, C. E., and Schusterman, R. J.), **211** (Appleton-Century-Crofts, 1968).

⁵ Fryer, T. B., and Deboo, G. J., in *Engineering in Medicine and Biology, Proc. Seventeenth Ann. Conf.* (Inst. Electrical and Electronics Eng., New York, 1964).

⁶ Kooyman, G. L., in *Antarctic Research Ser. II Biology of Antarctic Seas III*, **227** (American Geophysical Union, Washington DC, 1968).

Juvenile *Nephrops* caught in the Irish Sea

DIVING teams studying *Nephrops norvegicus* in Loch Torridon and the Sound of Jura have commented on the absence of small individuals with carapace lengths of less than 30 mm^{1,2}. Elsewhere in trawl samples, the shortest carapace is usually about 20 mm long³⁻⁵, although recent Irish and French research samples have found shorter, down to about 13 mm⁶⁻⁸. Extremely few post-larval or juvenile *Nephrops* smaller than this have been recorded; the wild-caught total summarized by Andersen⁹ and O'Riordan¹⁰ seems to be twelve, with an additional thirty-three taken from stomachs of *Raia clavata*⁹.

In June 1970 an experimental haul in the Irish Sea off County Dublin, with a small-meshed cover over the cod-end, yielded five early post-larvae and three stage 3 larvae. Following this, small-meshed covers were attached to the cod-end, the mid-point and to the base of each wing of the trawl, for routine

distribution surveys in October/November 1970 and in April and June 1971. This resulted in the capture of some specimens with a carapace length of well below 10 mm on each cruise.

Table 1 gives frequencies of different carapace lengths in the wing and cod-end cover catches for these cruises, with the June 1970 specimens for comparison. Numbers caught in covers naturally decrease with increasing size—50, 25 and 10% of the catch of the cod-end combined with its cover having carapace lengths of about 16, 18 and 20 mm respectively—but this transition is gradual enough to leave length-frequency modes relatively undisturbed.

Table 1 Summed Carapace Length-frequencies up to 22 mm of *Nephrops* in Small-meshed Covers on Wings (A) and Cod-end (B) of the Trawl in October/November 1970, and April and July 1971, together with Post-larvae of June 1970

Length of carapace (mm)	June 1970	October–November 1970		April 1971		July 1971	
		A	B	A	B	A	B
3	—	—	—	—	—	—	—
4	5	—	—	—	—	3	1
5	—	—	—	—	—	—	—
6	—	—	—	—	—	—	—
7	—	1	—	—	—	—	—
8	—	4	—	—	1	—	—
9	—	2	—	2	3	—	—
10	—	—	—	—	3	1	1
11	—	—	—	4	21	1	1
12	—	—	—	3	14	11	5
13	—	4	—	—	9	14	7
14	—	5	18	—	4	18	5
15	—	11	142	1	17	12	6
16	—	10	215	3	39	6	8
17	—	5	260	3	102	4	21
18	—	5	262	1	117	16	46
19	—	1	261	2	93	18	57
20	—	5	349	—	91	17	37
21	—	2	318	—	52	6	15
22	—	—	308	1	39	5	13

The resulting length-frequency distributions give strong indications of the growth-rate, the modal length in the 1970 year class increasing from 4 mm to 14 mm in a year, whilst that of the 1969 year class increases from approximately 16 mm in October to 19 mm the following July. The 1971 year-class is also represented in July 1971. An interesting feature of all surveys was the decreasing effectiveness of the covers on the wings relative to that on the cod-end as the size of the *Nephrops* increased. The genital pleopods were seen to be absent or tiny in October of the year of birth, but by the following April to have developed to the point where the sexual differences were just becoming distinguishable and to be moderately distinct by July.

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Received October 27, 1971; revised March 22, 1972.

- ¹ Anon., *Nature*, **229**, 298 (1971).
- ² Chapman, C. J., and Rice, A. L., *Marine Biol.*, **10**, 321 (1971).
- ³ O'Riordan, C. E., *Rapp. P.-v. Cons. Perm. Intern. Explor. Méditerran.*, **156**, 161 (1965).
- ⁴ Cole, H. A., *Rapp. P.-v. Cons. Perm. Intern. Explor. Méditerran.*, **156**, 164 (1965).
- ⁵ Thomas, H. J., *Rapp. P.-v. Cons. Perm. Intern. Explor. Méditerran.*, **156**, 176 (1965).
- ⁶ *Sea Fisheries Bulletin*, 1970, **7**, 5 (Dublin, 1969).
- ⁷ Abbes, R., and Warluzel, N., *Rev. Trav. Inst. Pêch. Marit.*, **34**, 5 (1970).
- ⁸ Hillis, J. P., *Fishery Leaflet*, **30** (Dublin, in the press).
- ⁹ Andersen, F. S., *Meddr. Danm. Fisk- og Havunders.*, **3**, 265 (1962).
- ¹⁰ O'Riordan, C. E., *Sci. Proc. Roy. Dublin Soc.*, **1**, **B**, 137 (1964).

Assortative Mating in Mice and the Incest Taboo

FEMALES from some inbred strains of *Mus musculus*, in a state of induced oestrus, when allowed to choose between a male of their own strain and another of a different strain, prefer to associate and mate with males of the different strain. This phenomenon was studied by Mainardi¹ in the C57BL and Swiss strains, and by us (ref. 2 and unpublished results) in the strains BALB/Ibg, DBA/Ibg, C57BL/Ibg, C57BL/J and C3H/J. Our study suggested the existence of a polymorphism for female mating preference, since females from the BALB/Ibg and C3H/J strains mated at random. Observations of the behaviour of females reared with foster fathers showed that a major determinant of mating preference is a "paternal effect". DBA/Ibg males, due to their genotype, provide social stimuli which induce a tendency in their daughters for mating preference for unlike males, whereas BALB/Ibg males do not induce any tendency for mating preference in their daughters.

Because female mating preference does not exist in all strains studied, it was advisable to study the distribution of the phenomenon in a genetically heterogeneous mouse population. Consequently we used the HS/Ibg stock, which is derived from an eight-way cross among inbred strains of mice, in the study described here. (More details on the origin of this stock are provided in ref. 3.) HS/Ibg litters were raised by both parents until they were 23 days old. At that time, two of the female offspring were placed in a small cage (23×11×10 cm high) in a separate room from their father until 2 weeks before testing. Another pair of daughters was reared in the company of their father in a large cage (32×21×10 cm high) until 1 day before testing. To prevent mating, the daughters were separated from the father by a hardware cloth barrier.

The preparation of the males and females for the experiment, the testing procedure, and the apparatus have been described before². Briefly, all animals were introduced to a reverse light cycle room when the females were 56 days old. Testing began 2 weeks later. During this time the females were given two treatments of oestrogen and progesterone injections and were habituated in a non-recording version of the testing apparatus for the 24-h period before testing. The testing apparatus consists of three clear plastic tubes, 4.4 cm in diameter, intersecting at equal angles. At each end of the three arms is fitted a standard housing cage (23×11×10 cm high) modified by an entry hole for the tube. A week before testing the males were fitted with a polyvinyl collar and a light bead chain. Twenty-four hours before testing, they were secured to their testing cages by the bead chains, and remained so for the duration of the experiment. In the test itself, a female in induced oestrus was allowed to choose between two males, whose sexual performance had been confirmed before testing. One of these males was the female's father and the other was the father of another female in the experiment. Each male participated in two mating preference tests in accord with a Latin square design. One test was with a daughter which had been raised with him only until weaning (short exposure) and the other was with a daughter which had been with him until 24 h before the testing day (long exposure). A week elapsed between tests.

A valid trial was defined as one during which either ejaculation occurred or the female stayed with one or both males for at least 1,200 s and two or more intromissions occurred. In addition, it was necessary that both males be sexually active. A male was regarded as non-active if, during the 1,200-s period with the female present in his cage, he failed to mount or intromit. If a mount without intromission occurred during the first 1,200 s, an additional 600-s period was provided within which he could intromit. When a test was regarded as invalid it was repeated within 2 days with the other female of the same exposure duration.

The following components of mating preference were measured: time of association with each male, number of

Table 1 No. of Females (N), Preference Ratios or Proportions (PR), and Results of Analysis of Variance of Exposure Effects

	Time of association †		No. of entries †		No. of intromissions †		First cage entered ‡		First male to intromit ‡		First male to ejaculate ‡	
	N	PR	N	PR	N	PR	N	PR	N	PR	N	PR
Short exposure	19	0.480	19	0.451	19	0.402	19	0.579	19	0.526	17	0.412
Long exposure	25	0.637*	24	0.560	24	0.760***	24	0.417	24	0.708*	22	0.818**
Exposure comparisons												
ANOVA					$P < 0.001$ ‡						$P < 0.01$ ‡	
ANOVA with repeated measures	$P < 0.05$ †		$P < 0.05$ †		$P < 0.05$ †							

* Deviations from 0.5 (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$).

† t test.

‡ χ^2 test.

entries into each male's cage, first cage entered, number of intromissions by each male, identity of the male that intromitted first, and identity of the male that ejaculated. Preference ratios were calculated for the continuous scores by dividing the scores for behaviour toward the unfamiliar males by the sum of the scores of both males. These scores were transformed (arc sin $\sqrt{\text{preference ratio}}$) before statistical analysis in order to normalize the distribution. The mean preference ratios for the continuous scores, the proportions for the nominal scores, the significance levels of the deviations from 0.5 (no preference), and the number of females tested are all given in Table 1. Since there was no test order effect, all scores were pooled within the same condition of length of exposure to father. Comparisons of the effects of duration of exposure were made using 2 by 2 χ^2 for the nominal scores. An analysis of variance for all the females and an analysis of variance with repeated measures, using only 15 available pairs for the continuous scores, were performed. The results are also presented in Table 1.

Females which stayed with their fathers until the day before testing preferred to associate and mate more with unfamiliar males. The females which had been reared with their fathers, however, only until weaning did not show any preference. These results contrast with those of females of some inbred strains and F_1 s which also were reared by their parents until weaning only, and which did show mating preference (ref. 2 and our unpublished results). A possible explanation is that members of the same inbred strain in the earlier experiments were reared until 56 days of age in the same breeding shelf, and thus in range of possible olfactory or auditory stimuli peculiar to the strain.

The "incest taboo", or avoidance of mating with relatives, is regarded as a near cultural universal in man⁴. Presumably behavioural mechanisms for the avoidance of inbreeding have evolved in many species (for example, in the white-throated sparrow⁵ and in the moth *Panaxia dominula*⁶). The present results not only suggest that such a mechanism exists in the mouse, but also offer a model of possible utility in studying the basis of the incest taboo in man.

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¹ Mainardi, D., *Atti Assoc. Genet. It.*, **9**, 141 (1964).

² Yanai, J., and McClearn, G. E., *Behav. Genet.*, **2**, No. 2/3, 173 (1972).

³ McClearn, G. E., Wilson, J. R., and Meredith, W., in *Contributions to Behavior-Genetic Analysis: The Mouse as a Prototype* (edit. by Lindzey, G., and Thiessen, D. D.) (Appleton-Century-Crofts, New York, 1970).

⁴ Lindzey, G., *Amer. Psychol.*, **22**, 1051 (1967).

⁵ Lowther, J. K., *Canad. J. Psychol.*, **39**, 281 (1961).

⁶ Sheppard, P. M., *Heredity*, **6**, 239 (1952).

Role for Protein Phosphorylation in Meiosis and in the Early Cleavage Phase of Amphibian Embryonic Development

DURING maternal embryogenesis, the vertebrate egg is blocked in meiotic prophase. At ovulation it proceeds to the metaphase of the second meiotic division, which is complete after fertilization or an artificial stimulus. The first mitotic division occurs about three hours later, and is followed by a series of rapid mitoses without cell growth. In amphibia, the cell cycle is completed in less than an hour at 180° C. During early cleavage in *Xenopus* there is reportedly¹ no G₁ phase, and the G₂ is either absent or very short.

We now report that the release of the prophase block at ovulation is associated with intense protein phosphorylation, and that the release of the metaphase block at fertilization coincides with protein dephosphorylation. Dephosphorylation continues at an exponential rate during early cleavage and appears to be associated with the doubling of DNA and/or cell number.

Rana pipiens were maintained from January to May in artificially induced hibernation at 4° C. Ovulation was induced by frog pituitary injection, and the eggs were stripped into a suspension of sperm in 0.1 Ringer's solution for fertilization. Clusters of 100–200 ovulated or fertilized eggs were taken for each sample at the times indicated in Fig. 1. Fifty to 100 fertilized eggs from each frog were allowed to develop to tailbud stage as controls. The results shown are from clutches of eggs showing 95% or better normal development.

Electrical recordings^{2,3} were made with the electrode tip 0.1–0.2 mm below the surface of the animal pole. A cell fraction containing the cortical pigment granules and the ouabain-sensitive, Na + K-activated, ATPase was isolated from a 0.24 M sucrose homogenate by differential centrifugation at 1,700g for 10 min after first removing the yolk platelets at 300g for 10 min as described before⁴. Calcium analyses were carried out on fuming nitric acid digests using atomic absorption spectroscopy⁴.

Thymidine-methyl-T (50 μ Ci) and/or H₃³²PO₄ (250 μ Ci) was injected into gravid females with the macerated pituitaries used to induce ovulation. Eggs were rinsed with distilled water and homogenized in five volumes of 7% trichloroacetic acid (TCA) at 4° C. The precipitate was washed with cold 7% TCA and extracted sequentially with CHCl₃:CH₃OH (2:1), CHCl₃:CH₃OH:HCl (2:1:0.001), 7% TCA at 90° C for 15 min, and 0.05 N NaOH at 100° C for 10 min. Aliquots of each

extract and the final residue were counted by liquid scintillation spectrophotometry. This report is concerned only with ^3H -thymidine incorporation into the hot TCA (nucleic acid) extract and ^{32}P incorporation into the alkali-labile (protein phosphorine) extract. Small amounts of ^{32}P -labelled phosphoproteins were recovered in both the $\text{CHCl}_3 : \text{CH}_3\text{OH}$ (crude lipid) and $\text{CHCl}_3 : \text{CH}_3\text{OH} : \text{HCl}$ (phosphoinositide) extracts but are not considered here.

Phosvitin was isolated as described for ling roe⁵, but was not separated on DEAE-cellulose into possible phosvitin subfractions.

The changes in membrane potential, calcium binding, protein phosphorylation and thymidine incorporation between meiotic prophase and the completion of the first mitotic cell division are compared in Fig. 1. The first one and one-half meiotic divisions are associated with membrane depolarization and a period of intense protein phosphorylation. Following fertilization the egg plasma membrane undergoes a transient positive-going hyperpolarization, approaching a plateau voltage of about +40 mV by the completion of meiosis (15–20 min). During the rising phase of the hyperpolarization there is a release of bound calcium and a partial protein dephosphorylation. The egg cytoplasm remains about 40 mV positive, relative to the external environment, until the completion of the first DNA synthetic period. As DNA synthesis ends, the egg membrane slowly repolarizes and first cleavage (mitosis) begins. Further step-wise dephosphorylations coincide with both the onset of DNA synthesis and with mitosis. By the completion of first cleavage the egg cytoplasm is again negative relative to the external environment.

Our data show that thymidine is incorporated into egg DNA

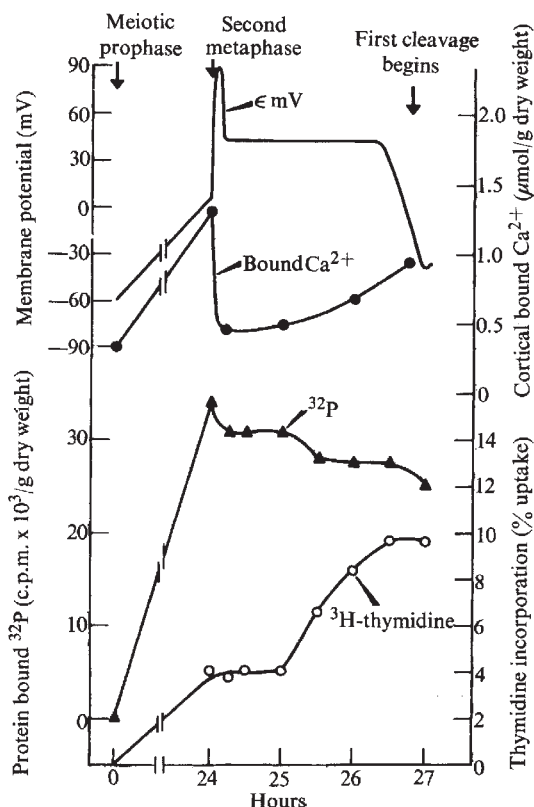


Fig. 1 Changes in membrane potential, calcium binding, protein-bound ^{32}P and thymidine incorporation between the terminal stage of first meiotic prophase (zero time on the abscissa) and first cleavage in *R. pipiens*. Fertilization occurred after 24 h. Membrane potentials and bound calcium are average values for five or more frogs. For further description and variations between eggs from the same and different frogs see ref. 2. ^{32}P and ^3H -thymidine incorporation are measured on sequential samples of ovulated and fertilized eggs from the same frog and are typical of four experiments.

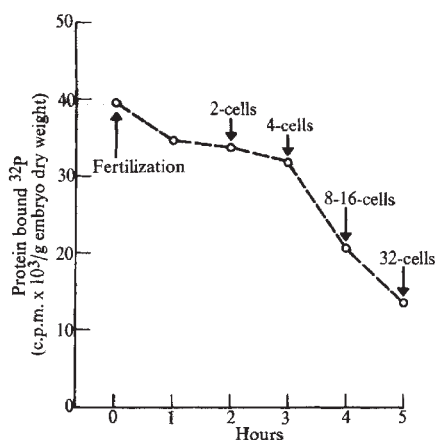


Fig. 2 Total protein-bound ^{32}P content of *R. pipiens* eggs between fertilization and the 32-cell stage. $^{32}\text{PO}_4$ was injected into gravid females as described in the text. Values shown are from sequential samples from the eggs of one frog and are representative of three experiments.

between the terminal stage of first meiotic prophase and second meiotic metaphase (Fig. 1). Periods of DNA synthesis have been detected by autoradiography during prophase in newt⁶, man⁷ and mouse⁸, and may occur at most stages of meiosis in *Trillium*⁹. In *Lilium*¹⁰, biochemical studies have shown a delayed replication of DNA during zygotene (stage 2, meiotic prophase), and repair associated with chiasma occurs during pachytene (stage 3, meiotic prophase). Synthesis of DNA has also been reported¹¹ to occur during pachytene in *Xenopus*. Our results suggest that DNA synthesis and/or repair also occurs between first meiotic prophase and second metaphase in *R. pipiens*.

We have previously shown³ that the prophase egg membrane is potassium selective in calcium containing medium but depolarizes and becomes sodium selective in calcium deficient medium. By contrast, the metaphase arrested (ovulated, unfertilized) egg membrane remains depolarized and sodium selective at all calcium concentrations. As calcium appears to act by decreasing the passive sodium permeability of the plasma membrane^{3,4}, ovulation must inhibit this calcium action at the egg surface. Similarly, fertilization removes the inhibition and again allows calcium to compete with sodium ion at the plasma membrane. As shown in Fig. 1, there is a four-fold increase in calcium-binding to the cortical granule-plasma membrane fraction during the protein phosphorylation at ovulation and a rapid loss of bound calcium during the dephosphorylation at fertilization. Preliminary experiments indicate that 30 to 35% of the total protein phosphate is localized in this fraction in the ovulated egg and that this protein phosphate is selectively released at fertilization. The cortical granule protein phosphate could serve as a calcium-sink, pulling calcium out of the plasma membrane with a resulting rise in intracellular sodium concentration and membrane depolarization. Protein dephosphorylation would result in the observed calcium release by the cortical granule fraction followed by a reaccumulation of calcium by the egg membrane and a net efflux of sodium from the fertilized egg.

The cell cycles remain well synchronized through the eight-cell stage. The protein-bound alkali-labile ^{32}P levels have been measured at one hour intervals over the first five mitotic cycles and have been found to decrease steadily (Fig. 2). The rate of phosphate loss approximately doubles for each successive mitotic cycle, suggesting that protein dephosphorylation is coupled to the increase in DNA and/or cell number. By the 32-cell stage approximately 65% of the total alkali-labile protein ^{32}P has been released.

The principal protein species phosphorylated between meiotic prophase and second metaphase appears to be the phosphoprotein, phosvitin. The specific activities of the total alkali-

Table 1 Incorporation of $^{32}\text{PO}_4$ into Total Alkali-labile Protein Phosphate and Purified Phosvitin between Meiotic Prophase and Second Meiotic Metaphase in *R. pipiens*

Preparation	Alkali-labile protein phosphate		
	$\mu\text{mols/dry weight embryo}$	$\text{c.p.m./}\mu\text{mol protein phosphate}$	Total protein ^{32}P
Total phosphoprotein	97.8	93	—
Purified phosvitin	16.6	304	56

labile protein phosphate and purified phosvitin isolated from metaphase arrested (ovulated, unfertilized) eggs are compared in Table 1. The specific activity of the purified phosvitin was 3.3 times that of the total protein phosphate, and even after losses during purification accounted for 56% of the total ^{32}P incorporated.

Protein kinase has been shown¹² to catalyse a reversible phosphate transfer between ATP and phosvitin. Essentially all of the more than 100 phosphoserine residues in phosvitin have an oxidation level equivalent to that of the enol phosphate derivative of phosphoserine¹³. Thus phosvitin may serve as a major energy store to be used during the cleavage phase of development.

Whether phosvitin is the protein undergoing reversible phosphorylation in the cortical granule fraction during meiosis and whether selective phosphorylation and/or dephosphorylation occurs at other specific sites within the egg during the different phases of development remain to be determined. This evidence indicates that the hormonal release of the prophase block coincides with the activation of protein kinase (possibly via cyclic AMP) and that the protein kinase is largely inactivated and/or the phosphate acceptor protein completely phosphorylated by second meiotic metaphase.

This work was supported in part by the National Institute of Child Health and Human Development. G. A. M. was a career scientist of the Health Research Council of the City of New York.

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- Graham, C. F., and Morgan, R. W., *Develop. Biol.*, **14**, 439 (1966).
- Morrill, G. A., and Watson, D. E., *J. Cell. Physiol.*, **67**, 85 (1966).
- Morrill, G. A., Rosenthal, J., and Watson, D. E., *J. Cell. Physiol.*, **67**, 375 (1966).
- Morrill, G. A., Kostellow, A. B., and Murphy, J. B., *Exp. Cell Res.*, **66**, 289 (1971).
- Mano, Y., and Lipmann, F., *J. Biol. Chem.*, **241**, 3822 (1966).
- Wimber, D. E., and Prenskey, W., *Genetics*, **48**, 1731 (1963).
- Lima-de-Faria, A., German, J., Ghatnekar, M., McGovern, J., and Anderson, L., *Hereditas*, **60**, 249 (1968).
- Mukherjee, A. B., and Cohen, M. M., *Nature*, **219**, 489 (1968).
- Riley, R., and Bennet, M. D., *Nature*, **230**, 182 (1971).
- Hotta, Y., Parchman, L. G., and Stern, H., *Proc. US Nat. Acad. Sci.*, **60**, 575 (1968).
- Gall, J. G., *Proc. US Nat. Acad. Sci.*, **60**, 553 (1968).
- Rabinowitz, M., and Lipmann, F., *J. Biol. Chem.*, **235**, 1043 (1960).
- Rosenstein, R. W., and Taborsky, G., *Biochemistry*, **9**, 649 (1970).

Mammary Stimulation causes Prolactin Secretion in Non-lactating Women

VARIOUS afferent neurogenic stimuli to the chest wall or breast have been associated with galactorrhoea in man. Non-puerperal lactation has been reported following mechanical trauma,

surgery, or burns of the chest wall or breast¹⁻⁴; following herpes zoster of the chest wall⁵; and induced by poorly fitting garments⁴ or breast manipulation^{3,4}. Lactation has occurred in men in association with prolonged suckling of the breast^{1,3} and may occur in nulliparous and post-menopausal women in response to a suckling stimulus^{5,6}.

Animal studies have demonstrated the importance of neuro-endocrine reflexes in the maintenance of lactation in several species⁷⁻¹¹. Severance of nerve pathways between the mammary glands and the central nervous system in the rat⁸, rabbit¹⁰, and cat⁹ blocks established lactation, although this response is not seen in sheep¹² or goats¹³. Marked rises in plasma prolactin levels have been reported in cows and goats both with lactation and with sham milking¹⁴. Pituitary prolactin content in lactating rats is influenced by extra-mammary neural stimuli as well as by suckling^{15,16}.

Reports have been made of elevated plasma prolactin levels in man in conditions of inappropriate lactation with diverse aetiologies¹⁷⁻²², but as yet there has been no demonstration of prolactin elevation in response to a reflex arc involving the breast or chest wall. Normal nursing does, however, cause a marked rise in serum prolactin in lactating women^{19,21}.

We report here that mechanical stimulation of the female breast will cause a marked rise in serum radioimmunoassayable prolactin, even in the absence of lactation. Some of the characteristics of this neural reflex have been defined.

Eight healthy adult women and seven healthy adult men were studied. The women's ages ranged from 21 to 28 yr (mean, 23.6); for men the range was 28 to 33 yr (mean, 30.7). None of the subjects had received any medication, including oral contraceptives, for at least one month before study. The past history of pregnancy and nursing and the interval since the last time of nursing for the women are indicated in Table 1.

Table 1 History of Pregnancy and Nursing in Women Subjects

Subject	Age (years)	Pregnancy history	History of nursing	Interval since last time of nursing (months)
1	22	G0 P0 Ab0	0	—
2	28	G2 P2 Ab0	+	40
3	24	G1 P1 Ab0	+	14
4	22	G1 P1 Ab0	0	—
5	21	G0 P0 Ab0	0	—
6	25	G1 P1 Ab0	0	—
7	23	G1 P0 Ab1	0	—
8	24	G1 P1 Ab0	+	17

All studies were performed between 0730 and 1000 h after an overnight fast. All subjects were tested in the sitting position. Samples were obtained after 5 min of sitting at rest, immediately following a 5 min period of self-stimulation of the left breast and nipple by manual manipulation, and 15 min following the cessation of self-stimulation; sera were promptly separated and stored frozen before assay. On subsequent occasions, the women were further tested (using the same sampling schedule) during manual self-stimulation of the breast without direct stimulation of the nipple or areolar area. Four of the women were tested by self-stimulation over the lower half of the sternum, and four of the women were tested during stimulation of the ventral surface of the left forearm. In addition, four of the women were tested during manual stimulation of the breast and nipple by their husbands, and four men were tested with manual stimulation of the breast and nipple by their wives.

HPr was measured using a highly specific mixed heterologous radioimmunoassay technique²². All samples for each set of stimulation conditions were measured in a single assay.

Serum HPr concentrations measured before and after self-stimulation of the breast and nipple for both males and females are shown in Fig. 1. The baseline HPr concentrations (men, mean $\pm$ s.e., 6.8 ± 0.5 ng/ml.; women, mean $\pm$ s.e., 5.1 ± 2.0 ng/ml.) were all within the normal range. Following self-

stimulation in the men, there was no significant change in serum HPr. Immediately after the 5 min period of self-stimulation of the breast and nipple in the women, however, serum HPr concentrations rose markedly (mean $\pm$ s.e., 108.1 ± 14.3 ng/ml.; range 43.5–168.0 ng/ml.). Fifteen minutes after self-stimulation, these values had returned towards normal, but were still elevated (37.4 ± 3.9 ng/ml.; range 14.5–54 ng/ml.).

Self-stimulation of the breast without direct stimulation of the nipple or areola in women also produced increases in HPr concentrations (Table 2), although the elevations were significantly less pronounced ($P < 0.005$, paired t -test). Manual self-stimulation of the lower half of the sternum and of the ventral surface of the left forearm produced no significant elevation in HPr concentrations (Table 2).

Table 2 Serum Prolactin Concentrations in Women before and after Sensory Stimulation

Stimulus site	Baseline	Immediately after stimulation	15 min after stimulation
Breast + nipple (N=8)	$5.1 \pm 2.0^*$	108.1 ± 14.3	37.4 ± 3.9
Breast alone (N=8)	5.8 ± 0.8	60.8 ± 4.3	22.6 ± 2.7
Sternum (N=4)	7.9 ± 1.8	7.1 ± 2.3	9.3 ± 1.4
Forearm (N=4)	9.5 ± 2.0	5.5 ± 0.3	5.8 ± 1.5

* Mean $\pm$ s.e., expressed as mg/ml. of serum.

Manual stimulation of the female breast and nipple by the woman's husband produced rises in HPr comparable to those obtained by self-stimulation ($P > 0.2$, Student's t -test). Values rose from a mean baseline level ($\pm$ s.e.) of 6.4 ± 1.3 ng/ml. to a mean peak concentration ($\pm$ s.e.) immediately following stimulation of 80.8 ± 16.6 ng/ml.; 15 min later HPr concentrations had fallen to 42.1 ± 5.5 ng/ml.

When the breast and nipple of the husband were stimulated by his wife, HPr concentrations rose from a baseline mean ($\pm$ s.e.) of 6.3 ± 1.3 ng/ml. to a mean ($\pm$ s.e.) peak of 24.5 ± 3.5 ng/ml. immediately following stimulation ($P < 0.001$, Student's t -test): this was contrary to the values gained from self-stimulation. Fifteen minutes after the end of stimulation, HPr levels were still elevated (mean $\pm$ s.e., 20.3 ± 3.5 ng/ml.).

No sexual arousal was reported by any of the men during either self-stimulation or stimulation by their wives. Three of the women reported moderate sexual arousal during stimulation of the breast and nipple when this was done by either themselves or their husbands; however, none of the women reported arousal with breast stimulation alone. Peak prolactin responses were similar in women with and without sexual arousal. Galactorrhoea was not observed in any subjects during these experiments.

Grimm³ postulated that stimulation of the fourth, fifth, and sixth intercostal nerves and their accompanying sympathetic fibres—the source of innervation of the breasts—may produce increased prolactin secretion in non-puerperal women and perhaps in men, resulting in galactorrhoea. Others have postulated increased prolactin secretion as a primary event in galactorrhoea due to persistent stimulation of a neural reflex arc^{1,2,4,23}. Elevation of HPr in nursing mothers after suckling has been demonstrated by radioimmunoassay^{19,21}. This report presents direct evidence for a neurally-mediated pituitary prolactin release in non-nursing women.

In these experiments, neither manual self-stimulation of the forearm nor of the lower half of the sternum resulted in appreciable changes in circulating prolactin concentrations. Marked increases in plasma HPr concentrations were, however, seen in women following stimulation involving the breast and nipple. These increases were comparable with self-stimulation or with stimulation by the woman's husband. Stimulation of the breast without direct stimulation of the nipple and areola produced increases of HPr that were consistently less than those obtained when nipple and breast were stimulated simultaneously.

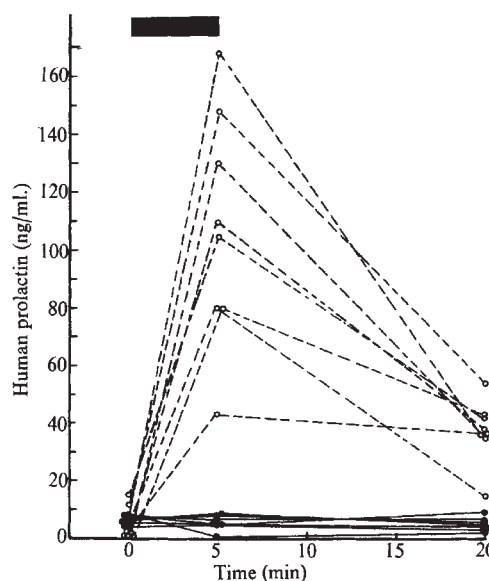


Fig. 1 Serum prolactin concentrations before and after self-stimulation of breast and nipple. ●—●, Men; ○---○, women; ■■■, period of breast and nipple stimulation.

The lower half of the sternum is innervated by the 4th–6th thoracic nerves, which also supply the breast. The breast, however, is more richly endowed with nerve endings than other tissue²⁴. Failure of stimulation of the sternum to produce elevations in HPr may be related to differences in threshold levels for activation of this reflex arc. Alternatively, there may be qualitative differences in skin receptors present at these two sites. In addition, the effect of psychological factors including the sexual significance of breast and nipple may play a role in modulating this response. Although direct stimulation of the nipple and areola is not necessary for release of prolactin by this reflex arc, it is difficult to assess the degree of indirect or spreading excitation of the nipple and areola which occurs with stimulation of the breast alone.

Although self-stimulation produced no HPr increase in males, stimulation by their wives resulted in a four-fold elevation of HPr. These results support the concept that psychological factors play an important role in this response.

This work was supported in part by a grant from the National Institute of Arthritis and Metabolic Diseases.

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- Salkin, D., and Davis, E. W., *J. Thoracic Surg.*, **18**, 580 (1949).
- Grossman, S., Buchberg, A. S., Brecher, E., and Hallinger, L. M., *J. Clin. Endocrin. Metab.*, **10**, 729 (1950).
- Grimm, E. G., *Quart. Bull. Northwestern Univ. Med. School*, **29**, 350 (1955).
- Barnes, A. B., *New Engl. J. Med.*, **275**, 1184 (1966).
- Slome, C., *J. Pediatr.*, **49**, 550 (1956).
- Mead, M., *Sex and Temperament* (Routledge, London, 1935).
- Selye, H., *Amer. J. Physiol.*, **107**, 535 (1934).
- Eayrs, J. T., and Baddeley, R. M., *J. Anat.*, **90**, 161 (1956).
- Beyer, C., Mena, F., Pacheco, P., and Alcaraz, M., *Fed. Proc.*, **21**, 353 (1962).
- Mena, F., and Beyer, C., *Amer. J. Physiol.*, **205**, 313 (1963).
- Mena, F., *Hormones and Behavior*, **2**, 107 (1971).
- Denamur, R., and Martinet, J., *Nature*, **185**, 252 (1960).
- Linzell, J. L., *Quart. J. Exp. Physiol.*, **48**, 34 (1963).
- Johke, T., *Endocrinol. Japon.*, **17**, 393 (1970).
- Mena, F., and Grosvenor, C. E., *Endocrin.*, **82**, 623 (1968).
- Moltz, H., Levin, R., and Leon, M., *Science*, **163**, 1083 (1969).

- ¹⁷ Forsyth, I. A., Besser, G. M., Edwards, C. R. W., Francis, L., and Myres, R. P., *Brit. Med. J.*, **3**, 225 (1971).
- ¹⁸ Kleinberg, D. L., and Frantz, A. G., *J. Clin. Invest.*, **50**, 1557 (1971).
- ¹⁹ Hwang, P., Guyda, H., and Friesen, H., *Proc. US Nat. Acad. Sci.*, **68**, 1902 (1971).
- ²⁰ Turkington, R. W., *J. Clin. Endocr.*, **34**, 159 (1972).
- ²¹ Bryant, G. D., and Greenwood, F. C., *Lactogenic Hormones* (edit. by Wolstenholme, G. E. W., and Knight, J.) (Churchill Livingstone, London, 1972).
- ²² Jacobs, L. S., Mariz, I. K., and Daughaday, W. H., *J. Clin. Endocr.* (in the press, 1972).
- ²³ White, A. E., *Ann. Intern. Med.*, **52**, 1264 (1960).
- ²⁴ Seto, H., *Studies on the Sensory Innervation* (Thomas, Springfield, Illinois, 1963).

Partial Suppression of Tumour Production by Dibutyryl Cyclic AMP and Theophylline

ADENOSINE 3',5'-cyclic monophosphate (cAMP) is the common intracellular mediator of a number of hormones and biogenic amines^{1,2}, and cyclic AMP or dibutyryl cyclic AMP (dbcAMP) also inhibits the growth of various lines of transformed fibroblasts and reverses their abnormal morphological characteristics toward normal without affecting the viability of the cells⁵. But, the effect of cAMP or dbcAMP treatment on the tumorigenicity of the transformed cells is not known. Here we describe an examination of the effect of dbcAMP treatment on the tumour-producing ability in hamsters by chicken-embryo-lethal orphan (CELO) virus-transformed hamster skin cells. The CELO virus is an endogenous adenovirus of chicken eggs, and is oncogenic when inoculated subcutaneously⁶ or intracerebrally⁷ in hamsters. It is also known to transform hamster embryo fibroblastic cultures⁸, hamster kidney cell cultures⁹ and hamster embryo skin cells *in vitro* (Pendola, R., Yates, V. J., Jasty, V., manuscript in preparation).

The small plaque variant of the Phelps strain CELO virus¹⁰ transformed hamster skin cells at hundredth passage (Pendola, R., Yates, V. J., Jasty, V., manuscript in preparation) were plated at 10⁵ cells/cm² and were grown in the presence of normal Hank's tissue culture medium, and another batch of cells were grown in the presence of Hank's medium containing 0.2 mM dbcAMP and 1 mM theophylline for 24 h and 48 h. One millilitre suspensions of 10⁶ cells were inoculated subcutaneously into 3- to 4-week-old female hamsters. Some of the cells, growing in the presence of dbcAMP and theophylline for 24 and 48 h, were washed with the normal medium, allowed to grow in normal medium for 24 h and then inoculated into hamsters. Some of the hamsters which received untreated transformed cells were subjected to theophylline treatment which inhibits phosphodiesterase¹² and thereby increases the endogenous concentrations of cAMP. The hamsters were examined daily for tumour development by palpation. After 3 to 5 weeks of tumour development, the animals were killed, tissues and sera were preserved and the tumours were fixed for optical and electron microscopic examinations. Hamsters that did not develop tumours were observed for 3 to 4 months.

All the hamsters which received untreated CELO virus transformed cells developed tumours within 12 to 15 days after inoculation. In hamsters that received transformed cells treated with dbcAMP and theophylline for 24 h, the incidence of tumour production was low and the incubation period was prolonged. Hamsters that received transformed cells treated with dbcAMP and theophylline for 48 h did not, however, develop tumours at all (Table 1). It has been shown *in vitro* that when cAMP-reversed transformed cells were transferred to normal media, they revert to the transformed state³. To test the tumour-producing ability of these retransformed cells, some of the cells that had undergone dbcAMP and theophylline treatment for 24 h or 48 h were allowed to grow in normal media for 24 h and then inoculated into hamsters. From Table 1, group numbers 4 and 5, it is clear that after growing

Table 1 Effect of Dibutyryl Cyclic AMP Treatment on Tumour-producing Ability of CELO Virus-transformed Cells in Hamsters

Treatment of cells	No. animals inoculated	No. animals developing tumour	%
1 Control untreated transformed cells	12	12*	100
2 24 h treatment dbcAMP (0.2 mM) and theophylline (1 mM)	8	3†	38
3 48 h treatment dbcAMP (0.2 mM) and theophylline (1 mM)	8	0	0
4 24 h with dbcAMP (0.2 mM) and theophylline (1 mM) 24 h with normal medium	5	4‡	80
5 48 h with dbcAMP (0.2 mM) and theophylline (1 mM) with normal medium	5	3§	60

* Incubation period 12 to 15 days.

† Incubation period 15 to 20 days.

‡ Incubation period 25 to 30 days.

§ Incubation period 40 to 50 days.

in normal media their tumour-producing ability was increased, although the incubation period was prolonged in proportion to the duration of the pretreatment with dbcAMP and theophylline. It seems that once the cells are reversed by a 48 h contact with dbcAMP, and then inoculated into the animal, the body cAMP concentration may itself be able to maintain the suppression of the tumorigenicity initially induced by dbcAMP. Even after 48 h contact with dbcAMP, however, when the transformed cells were grown in normal media for 24 h and then inoculated into the animals, they regained their tumour-producing ability to a lesser extent. Evidently, in that 24 h period in normal medium they regained their transformed characteristics, including the tumorigenicity.

Administration of theophylline itself into the animal significantly reduced the incidence of tumour production in hamsters by CELO virus-transformed cells (Table 2). Injection of theophylline on alternate days for one month from the day of inoculation of transformed cells was more effective than injection for only one week on alternate days. Hamsters, which already developed tumours, and were then subjected to theophylline treatment (Table 2, Group 4) had smaller tumours than those of untreated hamsters (Table 2, Group 1).

Table 2 Effect of Theophylline Treatment of Hamsters on Incidence of Tumour Production by CELO Virus-transformed Cells

Treatment of animals	No. of animals	No. developing tumours	%
1 Untreated animals	12	12	100
2 2 mg theophylline on alternate days for 4 weeks from first day of inoculation of transformed cells	6	1*	17
3 Theophylline given on alternate days for 1 week after administration of cells	5	3*	60
4 Theophylline was given on alternate days for 4 weeks after the tumour began to grow	6	6 (smaller in size)	

* The incubation period was longer than that of Group 1.

We also investigated the prophylactic effect of theophylline on hamsters for tumour production by CELO virus-transformed cells. Table 3 shows that administration of theophylline at shorter intervals for one or two days before the inoculation of the transformed cells increased the incubation period and reduced the incidence of tumour production. Because of its inhibitory effect on phosphodiesterase¹¹, theophylline increases the endogenous cAMP levels in hamsters, which in turn may induce the reversal effect on the transformed cells *in vivo*, as in *in vitro* observations.

Table 3 Prophylactic Effect of Theophylline in Hamsters for Tumour Production CELO Virus-transformed Cells

Treatment of animals	No. of animals	No. developing tumours	%
1 Untreated	12	12*	100
2 3 injections of 2 mg theophylline at 14 h intervals before the inoculation of transformed cells	9	5†	50

* The incubation period was 12 to 15 days.

† The incubation period was 15 to 21 days.

Cyclic AMP was thus shown to suppress the tumorigenicity of CELO virus-transformed hamster skin cells *in vivo*, and this was brought about first by pretreatment of the transformed cells with dbcAMP before inoculating them into the animal, and second by administration of theophylline to the animal after inoculation of the transformed cells.

We thank Dr V. J. Yates, Dr V. Jasty and Mr R. Pendola of the Animal Pathology Department of the University of Rhode Island for their help with tissue cultures.

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Received April 19, 1972.

- ¹ Robison, G. A., Butcher, R. W., and Sutherland, E. W., *Cyclic AMP* (Academic Press, 1971).
- ² Jost, J. P., and Rickenberg, H. A., *Ann. Rev. Biochem.*, **40**, 741 (1971).
- ³ Johnson, G. S., Friedman, R. M., and Pastan, I., *Proc. US Nat. Acad. Sci.*, **68**, 425 (1971).
- ⁴ Sheppard, J. R., *Proc. US Nat. Acad. Sci.*, **68**, 1316 (1971).
- ⁵ Heidrick, M. L., and Ryan, W. L., *Cancer Res.*, **30**, 376 (1970).
- ⁶ Sarma, P. S., Huebner, R. J., and Lane, W. T., *Science*, **149**, 1108 (1965).
- ⁷ Mancini, L. O., Yates, V. J., Jasty, V., and Anderson, J., *Nature*, **222**, 190 (1969).
- ⁸ Anderson, J., Yates, V. J., Jasty, V., and Mancini, L. O., *J. Nat. Cancer Inst.*, **42**, 1 (1969).
- ⁹ Anderson, J., Yates, V. J., Jasty, V., and Mancini, L. O., *J. Nat. Cancer Inst.*, **43**, 65 (1969).
- ¹⁰ Yates, V. J., Fry, D., Miller, L. T., and Jasty, V., *Infection and Immunity*, **2**, 118 (1970).
- ¹¹ Butcher, R. W., and Sutherland, E. W., *J. Biol. Chem.*, **231**, 1244 (1962).

Cross-reinnervation of Dystrophic Mouse Muscle

MUSCULAR dystrophy in mice is known to be genetically determined, as are certain forms of human muscular dystrophy¹⁻³. Whether the dystrophic condition is brought about by a primary lesion in the muscle fibres⁴⁻⁶ or by an abnormality of the "trophic" influence exerted by the motor neurones⁷⁻⁹ is uncertain. Significant experiments are those of McComas and Mrozek¹⁰, in which functional denervation of motor units in dystrophic mouse muscles was shown; and those of Salafsky¹¹, in which minced muscle from a normal donor failed to regenerate in a dystrophic host, while muscle from a dystrophic donor developed near-normal capabilities in a normal host. These experiments, among others, suggest that the motor neurones of dystrophic mice are abnormal in their ability to support muscle growth and to maintain functional contacts with the muscle fibres.

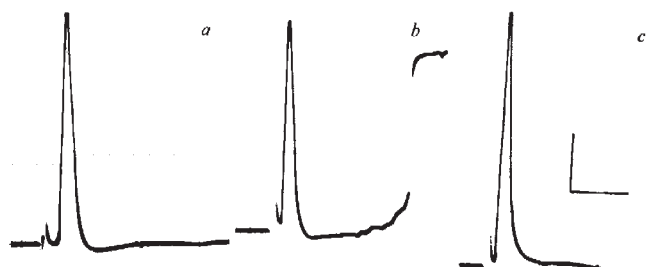


Fig. 1 Intracellular recordings of action potentials from fibres of (a) unoperated dystrophic soleus, (b) self-reinnervated dystrophic soleus and (c) cross-reinnervated dystrophic soleus. Records were taken 2 months after operation. Calibrations, 20 mV and 4 ms.

We have studied the properties of cross-reinnervated muscles of dystrophic animals, to test further the importance of neural trophic influences in dystrophic muscles. The motor nerves to "fast" and "slow" mammalian muscles exert specific trophic effects which govern the contractile and biochemical properties of the muscles¹²⁻¹⁶. In dystrophic mice, it is known that the "slow" muscles are less susceptible to dystrophy than the "fast" ones¹⁷⁻²⁰; but it is not known whether this difference arises from the different trophic effects of the motor nerves. The results reported here show that dystrophic muscles do not respond to cross-reinnervation in the same way as do normal muscles.

The experiments were carried out with 6-7 week old mice of the Bar Harbor 129/ReJ-dy strain. After ether anaesthesia the soleus (SOL) muscle in the right leg of the mouse was exposed, and to avoid self-reinnervation of the muscle, about 3 mm of the nerve that supplied the SOL was removed. The nerve innervating the flexor digitorum longus was gently pulled out of that muscle and laid around the SOL, providing sufficient nerve for implantation. The nerve distal to the point where it had been pulled degenerated in time but provided the necessary mechanical guidance²¹⁻²² to direct the regenerating portion of the nerve to innervate the SOL muscle. Thus the conventional "gluing"¹⁵ and "suturing"¹⁶ of the nerve to the muscle were avoided. As a control, the left SOL was reinnervated with its own nerve after the latter had been severed at its point of entry into the muscle. Similar operations were performed on normal littermates of the dystrophic mice.

In normal mice, functional neuromuscular contacts were established 6 weeks after cross-reinnervation, confirming the findings of Saito and Zacks²³. Similarly, with acetylcholinesterase staining²⁴, newly-formed end-plates were found in the cross-reinnervated and the self-reinnervated dystrophic SOLs 6 weeks after the operation. End-plates so formed were functional, because the muscle contracted when the motor nerve was stimulated. Action potentials were recorded with intracellular micro-electrodes from the reinnervated muscle fibres; these were very similar in amplitude and duration to those recorded in the unoperated dystrophic SOL (Fig. 1).

In the normal rat it has been reported that reinnervation of a "slow" muscle (for example, SOL) by the motor nerve previously supplying a "fast" muscle (for example, flexor digitorum longus) alters the contractile properties of the reinnervated muscle fibres so that they resemble more closely those in the "fast" muscle¹². Our results for mice, obtained from thirteen normal littermate controls, were similar. Contractions of isolated muscles²⁵ were measured isometrically using an RCA 5434 force transducer²⁶. The mean contraction time of the cross-reinnervated normal SOLs was about half that of the self-reinnervated ones 2.5 months after reinnervation (see Table 1 and Fig. 2). In dystrophic mice, however, only one out of the ten cross-reinnervated SOLs developed a significantly shorter contraction time. SOL muscles in the remaining animals did not show any significant change in contraction time from their respective self-reinnervated controls (see Table 1 and Fig. 2).

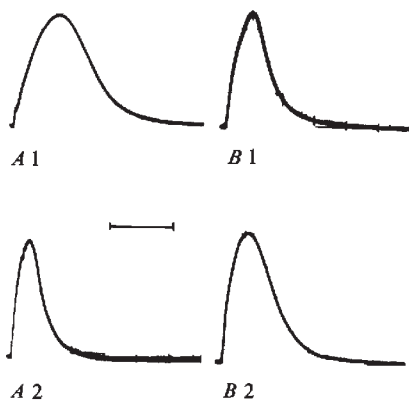


Fig. 2 Isometric contraction responses to a single maximal shock applied to the motor nerve: A1, self-reinnervated normal soleus; A2, cross-reinnervated normal soleus; B1, self-reinnervated dystrophic soleus; B2, cross-reinnervated dystrophic soleus. All records were obtained 2.5 months after operation when the animals were 4.5 months old. Experiments were done at 37° C. Time scale is 40 ms.

The mean contraction time of the self-reinnervated dystrophic SOLs did not differ statistically from that of the self-reinnervated normal SOLs (Table 1).

The effect of cross-reinnervation on membrane properties of the muscle fibres was also studied. The membrane "cable" constants of the muscle fibres were determined, using methods reported elsewhere²⁵. The results are summarized in Table 1.

In the normal animal, the fibres of the SOL muscle have higher membrane resistance than those of the fast extensor digitorum longus (EDL). In dystrophic animals, SOL fibres have lower than normal membrane resistance²⁵, whereas EDL fibres have higher than normal membrane resistance. Apparently the two muscles react differently to dystrophy.

Cross-reinnervated SOL fibres in the normal mouse show membrane properties approaching those of the EDL fibres, whereas self-reinnervated SOL fibres have membrane properties similar to those in unoperated muscles. In contrast, the

Table 1 Effect of Cross-reinnervation on Contraction Time and "Cable" Properties of Normal and Dystrophic Mouse Soleus Muscles

Muscle	CT (ms)	N'	R _{in} (K)	R _i (cm)	d (μm)	R _m (cm ²)	N
SOL							
Normal			535 ±176	50 ±10	30 ±8	1,516	113
Self-reinnervated normal	25 ±3	13	482 ±109	61 ±17	32 ±8	1,243	28
Cross-reinnervated normal	13 ±3	13	283 ±100	69 ±17	36 ±9	544	66
EDL							
Normal	9 ±3	12	217 ±63	58 ±10	34 ±8	304	124
SOL							
Dystrophic			234 ±89	50 ±10	39 ±9	636	131
Self-reinnervated dystrophic	20 ±7	10	268 ±104	65 ±15	41 ±11	752	45
Cross-reinnervated dystrophic	20 ±6	10	263 ±94	59 ±12	38 ±10	635	80
EDL							
Dystrophic	10 ±2	5	267 ±118	68 ±17	45 ±13	969	62

Mean values ± s.d. are given. R_{in}, input resistance; R_i, sarcolemmal resistivity; d, fibre diameter; R_m, specific membrane resistance, calculated from $\pi^2 d^3 R_{in} / 2 R_i$; CT, contraction time; N', number of muscles used for CT measurements; N, number of fibres used for cable property measurements.

shift in membrane properties is not found in cross-reinnervated dystrophic SOL muscle fibres; values for cable constants were not markedly different in cross-reinnervated and self-reinnervated dystrophic SOLs.

The fact that the contraction times and the fibre cable constants were not significantly altered in cross-reinnervated dystrophic SOLs suggests that some neural trophic factors present in normal mice are missing in dystrophic mice, or that dystrophic muscle is not able to respond to the trophic factor(s). The latter possibility seems unlikely, as it has been shown that dystrophic muscle could develop near normal properties in a non-dystrophic host¹⁴. The neural trophic effect, present early in the life of the dystrophic animal and accounting for the differentiation of fast and slow muscles, may become weaker as the animal ages. A weak neural trophic influence in dystrophic mice as compared with the normal mice might be a primary, genetically determined event in mouse muscular dystrophy. The work of Harris and Wilson⁸⁻⁹ also pointed to a deficiency in motoneurons of dystrophic muscles.

This work was supported by a research grant from the Muscular Dystrophy Association of Canada and by a National Research Council of Canada scholarship and a University of Toronto (Ramsay Wright) scholarship awarded to P. K. L.

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Received January 3; revised April 11, 1972.

- Michelson, A. M., Russell, E. S., and Harman, P. J., *Proc. US Nat. Acad. Sci.*, **41**, 1079 (1955).
- Baker, N., Blahad, W. H., and Hart, P., *Amer. J. Physiol.*, **193**, 530 (1958).
- West, W. T., and Murphy, E. D., *Anat. Res.*, **137**, 279 (1960).
- Harman, P. J., Tassoni, J. P., Curtis, R. L., and Hollinshead, M. B. (edit. by Bourne, G. H., and Golarz, M. N.), 407 (Karger, New York, 1963).
- Pearce, G. W., and Walton, J. N., *J. Path. Bacteriol.*, **86**, 25 (1963).
- Meier, H., West, W. T., and Hoag, W. G., *Archs. Pathol.*, **80**, 165 (1965).
- McComas, A. J., Sica, R. E. P., and Currie, S., *Nature*, **226**, 1263 (1970).
- Harris, J., and Wilson, P., *Nature*, **229**, 61 (1971).
- Harris, J. B., and Wilson, P., *J. Neurol. Neurosurg. Psychiat.*, **34**, 512 (1971).
- McComas, A. J., and Mrozek, K., *J. Neurol. Neurosurg. Psychiat.*, **30**, 526 (1967).
- Salafsky, B., *Nature*, **229**, 270 (1971).
- Buller, A. J., Eccles, J. C., and Eccles, R., *J. Physiol.*, **150**, 417 (1960).
- Close, R., *Nature*, **206**, 831 (1965).
- Miledi, R., Stefani, E., and Zelena, J., *Nature*, **220**, 497 (1968).
- Fex, S., and Jirmanova, I., *Acta Physiol. Scand.*, **76**, 257 (1969).
- Guth, L., Samaha, F. J., and Albers, R. W., *Expl. Neurol.*, **26**, 126 (1970).
- Brust, M., *Amer. J. Physiol.*, **210**, 445 (1966).
- Rowe, R. W. D., and Goldspink, G., *J. Anat.*, **104**, 531 (1969).
- Harris, J. B., *J. Neurol. Sci.*, **12**, 45 (1971).
- Cosmos, E., *The Muscular Dystrophy News*, Fall (1970).
- Weiss, P., *J. Exp. Zool.*, **100**, 353 (1945).
- Mark, R. F., *Brain Res.*, **14**, 245 (1969).
- Saito, A., and Zacks, S. I., *Exp. Molec. Pathol.*, **10**, 256 (1969).
- Ginsborg, B. L., and Mackary, B., *Biblphie Anat.*, **2**, 174 (1960).
- Law, P. K., and Atwood, H. L., *Expl. Neurol.*, **34**, 200 (1972).
- Atwood, H. L., Hoyle, G., and Smyth, T., *J. Physiol.*, **180**, 449 (1965).

Dextrans and Fibrin Morphology

THROMBIN clotting time is accelerated in the presence of small amounts of dextran¹, although dextran has a significant anti-thrombotic effect². To resolve this paradox Dhall and Bryce³ used a turbidimetric technique to examine the clotting of platelet-poor plasma by thrombin, and showed that small amounts of dextran shortened the induction phase before the appearance of fibrin, accelerated the development of turbidity

and enhanced its equilibrium value. They concluded that the structural inhomogeneities normally developed during clotting are rendered coarser in the presence of dextran. We have examined the effect of dextran during the clotting of purified fibrinogen in artificial media; turbidimetric and ultrastructural studies on such fibrin clots confirm the predictions made on the basis of physico-chemical studies. We have made turbidimetric measurements during the clotting of platelet-poor plasma after dextran infusion in man, and these suggest that dextran has a similar action *in vivo*.

Two millilitre aliquots of human fibrinogen (Behringwerke, AG) dissolved in 0.895% NaCl at a concentration of 1.5 mg per ml. were placed in siliconized cuvettes. Into this was mixed 0.2 ml. of either 0.895% NaCl alone, or dextran dissolved in 0.895% NaCl. Dextran fractions (m.w. 10,000–776,000) used for these experiments were made up as solutions over a range of concentrations from 0.25–20%. Freshly thawed thrombin (Parke, Davis and Co.) solution at a final concentration of 0.25 NIH units per ml. was then added into the cuvette and mixed for 10 s. A 'Unicam SP 800' spectrophotometer was used to measure the turbidity at 608 nm and 350 nm for 30 min after the addition of thrombin. In separate experiments fibrin clots made with and without dextran were matched according to the central illumination test⁴ against a range of mixture in different proportions of paraxylene (refractive index 1.4949) and methyl naphthalene (refractive index 1.6143), using an ordinary light microscope. The refractive indices of the matched mixtures were measured with an Abbé refractometer. In a third series of experiments, fibrin clots made with and without dextran were prepared for electron microscopy using the epoxy resin embedding technique. The grids were viewed in a Siemens 'Elmiskop 1A' at magnifications up to 30,000.

Two normal men were infused with 500 ml. of a 6% solution of dextran m.w. 70,000 ('Macrodex') in isotonic saline and 2 male surgical patients were given 500 ml. of a 10% solution of dextran m.w. 40,000 ('Rheomacrodex') in isotonic saline. Platelet-poor citrated plasma, prepared as previously described³, before and 4 h after the infusion was clotted with 0.25 NIH units thrombin and turbidity measured.

The turbidimetric changes accompanying the clotting of purified fibrinogen by thrombin show three distinct phases (Fig. 1)—an initial lag or induction phase, a phase of rapidly increasing turbidity and a third phase of slowly increasing turbidity lasting many hours. Dextran modified all three phases: the induction phase was diminished, the development of turbidity during the second phase was accelerated and the equilibrium turbidity was enhanced. A similar effect of dextran was found during the clotting of fibrinogen by thrombin in the presence of calcium. This action was observed with all fractions of dextran over the examined range (m.w. 10,000–776,000) and seemed independent of the molecular weight, but increased as the concentration of dextran is increased. These changes are similar to those described during the clotting of platelet-poor plasma in the presence of dextran added *in vitro*³.

The quantitative relationship between the wavelength of incident light and turbidity of a suspension of spherical particles is given by the Rayleigh-Gans equation⁵. For turbidity (T_1 and T_2) of the same solution at two different wavelengths (λ_1 and λ_2) this equation may be modified and written as

$$\frac{T_1}{T_2} = \left(\frac{\lambda_2}{\lambda_1}\right)^4$$

If the size of the particle is small compared with the wavelength of the incident light, then the ratio of turbidities, the opacity ratio, may be predicted from the known wavelengths. For 350 and 608 nm the ratio should be 9.1. The larger the inhomogeneities formed, the smaller the opacity ratio will become. It was found that during the clotting of purified fibrinogen the opacity ratio in both the control and dextran samples declined within the range of 8.5 to approximately 1.81.

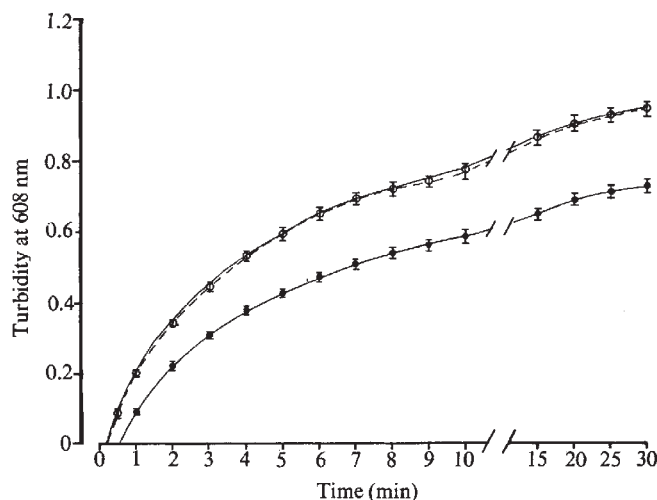


Fig. 1 Changes in turbidity of fibrinogen solution (1.5 mg per ml.) during clotting with thrombin (0.25 units per ml.) in presence of dextran (molecular weight 40,000) (O—O), dextran (molecular weight 70,000) (O---O), both at a final concentration of 0.9% in 0.895% NaCl solution alone (●—●). Mean of 5 with 1 s.d.

Table 1 shows the effect of dextran, of molecular weight 70,000, on the opacity ratio in purified fibrinogen solution. In each instance the presence of dextran decreases the opacity ratio. This indicates that the structural inhomogeneities developed during clotting are much larger in the presence of dextran and as the concentration of dextran is increased the inhomogeneities also increase.

Table 1 Changes in Opacity Ratio

Additive	Final concentration %	Opacity ratio
NaCl	—	2.30
Dextran	0.23	2.27
Dextran	0.45	2.15
Dextran	0.90	2.00
Dextran	1.80	1.81

Effect of 0.895% NaCl or of different concentrations of dextran (molecular weight 70,000) on opacity ratio, that is, the ratio of turbidity at 350 nm and 608 nm. The values shown are those during third phase of turbidity (see text) 30 min after the addition of thrombin at a final concentration of 0.25 units per ml.

Electron micrographs of fibrin clots made *in vitro* with and without dextran at a final concentration of 0.9% show that profound differences are induced in fibrin morphology by dextran. Fibrin fibres are rendered variable in size and coarser than normal. In addition, the clot contains amorphous structures lacking in cross-striation pattern. This finding accords with the higher opacity ratio obtained for such clots.

It is uncertain whether infusions of dextran result in such major alterations in fibrin clots. Dextran fractions of this molecular weight (70,000) are, however, in wide clinical usage for plasma volume expansion and for its anti-thrombotic effect. The final concentration at which changes are pronounced *in vitro* are within pharmacological range. Furthermore, thrombin clotting time is shortened after dextran administration⁶ and our recent studies (Table 2) show that the opacity ratio measured in platelet-poor plasma after dextran infusion in man is decreased. This suggests that dextran alters the structure of fibrin clots formed after infusion. Although effects of such alterations in clot morphology are speculative, it is possible that such major changes in fibrin structure and architecture result in alterations in biophysical properties of fibrin clots. Of particular interest in this respect is the clot mechanical strength and clot porosity. A permeable clot

Table 2 Effects of 'Macrodex' and 'Rheomacrodex' on Opacity Ratio

Pre-infusion	4 h post-infusion
2.58 *	2.10
2.62 *	2.21
2.18 †	1.80
2.32 †	1.86

Effect on opacity ratio of an infusion of 500 ml. of a solution of 6% dextran (molecular weight 70,000) ('Macrodex') in isotonic saline and 10% dextran (molecular weight 40,000) ('Rheomacrodex') in isotonic saline. Measurements of turbidity were made at 350 nm and 608 nm, before and 4 h after the infusion. The values shown are derived from those 30 min after the addition of thrombin at a final concentration of 0.25 units.

* Healthy subjects infused with dextran m.w. 70,000.

† Surgical patients infused with dextran m.w. 40,000.

would presumably undergo more ready dissolution with fibrinolytic agents. This and similar areas are being studied. It is clear, however, that the anti-thrombotic action of dextran² might lie in its ability to induce morphological changes in fibrin.

We thank Pharmacia AB for financial assistance and for dextran fractions.

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Received March 20, 1972.

¹ Laurell, A. B., *Scand. J. Clin. Lab. Invest.*, **3**, 262 (1951).

² Lambie, J., Barber, D., Dhall, D. P., and Matheson, N. A., *Brit. Med. J.*, **2**, 144 (1970).

³ Dhall, D. P., and Bryce, W. A. J., *Proc. Sixth Europ. Conf. Microcirc.*, 375 (1971).

⁴ Gay, P., *Introduction to Crystal Optics*, 64 (Longmans, Green and Co. Ltd, London, 1967).

⁵ Heller, J., *Chem. Phys.*, **26**, 920 (1957).

⁶ Nilsson, I. M., and Eiken, O., *Thromb. Diath. Haemorrh.* (Stuttgart), **11**, 38 (1964).

Changes in the Fibre Content of the British Diet

In nineteenth century Britain, the main dietary sources of "fibre" were cereals, potatoes and, to a lesser extent, green vegetables and pulses. The widespread introduction of roller milling between 1877 and 1880, followed by the growth of the food processing industry and changes in technology, is often said to have resulted in a marked decrease in the amounts of cellulose and other forms of indigestible fibre or "roughage" in the national diet during the past 100 yr. Moreover, the continued ingestion of a low "fibre" diet has been linked with a variety of diseases which occur predominantly in economically-developed Western countries, and which have become more common in Britain during this century. These include appendicitis¹, toxæmia of pregnancy¹, diverticular disease, and cancer of the colon and rectum³⁻⁵, as well as changes in the levels of serum triglycerides and serum cholesterol⁶. Here I examine whether there has been a concomitant decline in the average "fibre" content of the British diet. This can only be assessed in terms of crude fibre which is an imprecise index of those carbohydrates in plant foods which are not digested by man.

Changes in social structure and agricultural development during the eighteenth and early nineteenth centuries make it desirable to examine the fibre content of the diet at that time, but because of the great variations between the foods eaten by the labouring classes and the wealthy, and between the diets of people in towns and in scattered rural areas⁸⁻¹⁰, the concept

of "average food intake" has little meaning; early estimates of fibre intake are therefore tentative.

By 1700, wheat had largely replaced rye and barley for breadmaking, and there was already a growing demand in south and east England for fine white bread¹¹. In Scotland, on the other hand, bread was frequently made from oatmeal only¹².

Analyses by Lawes and Gilbert of the ash in wheat samples processed in a commercial water mill, coupled with subsequent work by the Research Association of British Flour Millers on wheats processed in different types of mill, suggest that the fibre content of stone-ground flour in the mid-19th century was between 0.2 and 0.5% (J. B. Hutchinson, personal communication). Wheat flour consumption in 1835 was about 360 lb per person per annum¹³, thus bread would have provided between 0.9 and 2.2 g fibre daily. Oatmeal contains about 1% fibre¹⁴ so that 2 pints of porridge provide a little under one gram; it therefore seems probable that the influence of oatmeal on the fibre content of the diet of the poorer classes may sometimes have been over-emphasized.

Between 1850 and 1890, changes in milling techniques caused a gradual decline in the fibre content of white wheat flour; this trend was stimulated by the increasing use of "hard" wheats and competition from imported "strong" white flours which accentuated the importance of whiteness. The introduction of silk bolting cloths which allowed better separation of the finer particles of bran (i.e. the pericarp, seed coat and aleurone layer of the grain), the advent of roller milling and the introduction of purifiers all contributed to this change.

The fibre content of the national diet in the period immediately preceding the introduction of roller milling cannot be measured, but the approximate amount in a farm labourer's diet in 1863 can be estimated from food consumption data from 370 farm labourers' families throughout England¹⁵. The average consumption of "breadstuffs" was 12½ lb per head per week. White flour ("seconds") was preferred and in only one case was whole brown meal used. Assuming "white" stone-ground flour contained 0.2 to 0.5% fibre, the daily intake from this source would be 1.1-2.8 g. Except in the northern counties, oatmeal, barley and rye were used only in small amounts. The average potato consumption by an adult was 6 lb weekly from which a further 1.3 g fibre would be derived, making a total of 2.4-4.1 g per head per day. Green vegetables were eaten spasmodically when potatoes were scarce; fruit was not mentioned in the dietary records.

The overall changes in the fibre content of the diet during the past century can be examined in greater detail. From 1909-13 onwards the quantities of the main fibre contributing foods (Table 1) can be derived from national statistics relating to total food supplies for the population as a whole¹⁶⁻¹⁸. The earlier data¹⁹ refer only to wheat flour and potatoes.

Table 1 United Kingdom Food Supplies (lb per Head per Annum)

	1880 *	1909-13 †	Pre-War II ‡	1942 †	1944 †	1957 †	1970 ‡
Potatoes	296	243	190	225	275	224	224
Other vegetables (including tomatoes)	NA	78	128	139	140	136	147
Fruit and nuts	NA	68	126	80	85	121	126
Wheat flour	280	211	194	227	234	172	145
Grain products (including wheat breakfast cereals)	NA	26	16	19	19	15	18

NA, Not available.

* See ref. 19.

† See ref. 17.

‡ See ref. 18.

§ See ref. 16. The report contains little detail about types of fresh vegetables and fruit.

Table 2 Fibre Content of the British Diet

	1860	1880	1909-13	Pre-World War II	1942	1944	1957	1970
Total fibre (g per head per day)	(2.4-4.1)	2.1 *	3.6	3.8	5.3	5.0	4.2	4.2
Potatoes	(1.3)	1.25	1.03	0.80	0.95	1.16	0.94	0.94
Other vegetables (including tomatoes)	NA	NA	1.11	1.40	1.45	1.48	1.58	1.62
Fruit and nuts	NA	NA	0.62	1.10	0.84	0.81	1.03	1.10
Wheat flour	(1.1-2.8)	0.85	0.58	0.46	1.92	1.30	0.46	0.39
Grain products	NA	NA	0.30	0.06	0.19	0.20	0.14	0.15
% Contribution from:								
Vegetables			59	57	45	53	61	61
Fruit and nuts			17	29	16	17	25	26
Cereals			24	14	39	30	14	13

NA=Not available. * Refers only to fibre from potatoes and wheat flour (1860). Approximate figures for the diet of farm labourers in England.

Changes in the fibre content of the national diet are summarized in Table 2. The total fibre in each food group can be compared in different years, but the absolute levels of intake should be regarded with caution, because the accuracy of the analytical method is generally regarded as only $\pm 0.05\%$ even at the lower ranges. As few British data are available for foods other than flour (see Table 3), published values from other sources²⁰⁻²² were used for most foods with an allowance being made for inedible material. More recent methods of fibre analysis give higher results in some instances; the fibre content of modern cultivars of some vegetables and fruits may in addition be lower and this has not been allowed for. Nevertheless it is apparent that there has been very little change in the total fibre in the average diet even from before 1880, apart from a slight upward trend in the early years of World War II.

Table 3 Data Used to Calculate the Fibre Content of Flours

			Fibre %
1860	'White', stone-ground (68-80% extraction)	0.2-0.5 *	
	Wholemeal, stone-ground	2.1 †	
1880	White, roller (70-73% extraction) milled	0.15 † (<0.1-0.2)	
	Wholemeal, roller milled	2.1 †	
1909-13	White (70-72% extraction)	0.15 †	
	Brown (90-95% extraction)	1.5 † (1.4-1.6)	
	Wholemeal	1.85 † (1.6-2.1)	
1939	White (70-72% extraction)	0.15 †	
	Wholemeal	1.85 †	
1942	National (85% extraction)	0.68 § (10 months average 0.7; 2 months average 0.55)	
1944	National (82.5-85% extraction)	0.45 § (9 months average 0.5; 3 months average 0.31)	
1957, 1970	White (70-72% extraction)	0.15	
	Wholemeal	1.85	
	Off-white (75-80% extraction)	0.2 †	
	Brown	1.5	

* Personal communication from J. B. Hutchinson.

† See ref. 23.

‡ See ref. 24.

§ See refs. 25-29.

The available data suggest that the "white" bread which was widely eaten in southern Britain in the 1860s only provided between 1 and 3 g fibre in the average diet, in contrast to wholemeal bread which if eaten in the same quantity would have supplied 9-12 g.

The compulsory use of a high extraction rate for all flour caused by shortages of wheat in 1918, in World War II and for a short period in 1946 was accompanied by increases in the amount of cereal fibre in the diet but, with these exceptions, the decline in the average consumption of bread and flour led to a gradual fall in the amount of cereal fibre ingested in the period under review. An increase in the fibre contribution from fruit and vegetables (other than potatoes) since World War II has also led to a decline in the relative importance of cereal fibre. Thus while flour and grain products contributed a quarter of the total fibre in the diet in 1909-13, by 1970 the proportion was only 13%.

The introduction of roller milling does not appear to have led to a significant decline in the fibre content of the diet at the end of the nineteenth century. Furthermore, in the different periods for which detailed consumption data are available, the greatest variation in daily intake was only about 2 g. While there has been very little alteration in the amount of fibre in the national diet in the past 100 yr, it may be of importance that the main sources of fibre have changed.

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Received April 20; revised May 24, 1972.

- Rendle-Short, A. S., *Brit. J. Surg.*, **8**, 171 (1920).
- Hipsley, E. H., *Brit. Med. J.*, **2**, 420 (1953).
- Burkitt, D. P., *Lancet*, **ii**, 1229 (1969).
- Burkitt, D. P., *Cancer*, **28** (1), 3 (1971).
- Painter, N. S., and Burkitt, D. P., *Brit. Med. J.*, **2**, 450 (1971).
- Eastwood, M., *Lancet*, **ii**, 1222 (1969).
- Holder, Dodds, E. C., and Moran, T., in *Bread*, 30 (Constable, London, 1954).
- Drummond, J. C., and Wilbraham, A., *The Englishman's Food* (2nd ed. by Hollingsworth, D. F.) (Jonathan Cape, London, 1957).
- Burnett, J., *Plenty and Want* (Thomas Nelson, London, 1966).
- Barker, T. C., McKenzie, J. C., and Yudkin, J., *Our Changing Fare* (Macgibbon and Kee, London, 1966).
- McCance, R. A., *Lancet*, **ii**, 205 (1955).
- Accum, F., *Treatise on the Art of Making Good and Wholesome Bread of Wheat, Oats, Rye and other Farinaceous Grain* (Thomas Boys, 1821).
- Lloyd, E. M. H., *J. Agric. Econ. Soc.*, **4**, 89 (1936).
- Moir, H. C., in *The Nation's Food* (edit. by Bacharach, A. L., and Rendle, T.), 210 (Society of Chemical Industry, London, 1946).
- Smith, E., *The Food of the Poorer Labouring Classes in England*, Sixth Report of the Medical Officer of the Privy Council, 1863. Appendix 6 [3416], HC 1864 XXVIII, 216.
- Royal Society Committee, *The Food Supply of the United Kingdom Cd. 8421* (HMSO, London, 1917).
- Ministry of Agriculture, Fisheries and Food, *Bd. Trade J.*, **183**, i (1962).
- Ministry of Agriculture, Fisheries and Food, *Trade and Industry*, **4**, 90 (1971).
- Levi, L., Bourne, S., Brittain, T., Hancock, Jevons and Fellows, F. P., *Report of the Fifty-first Meeting of the British Association for the Advancement of Science*, 272 (John Murray, London, 1882).

- ²⁰ Watt, B. C., and Merrill, A. L., *Composition of Foods: Agriculture Handbook No. 8* (Agricultural Research Service, United States Department of Agriculture, Washington, DC, 1963).
- ²¹ Food and Agriculture Organization, *Food Composition Tables for International Use* (FAO Nutritional Studies No. 3, Washington, 1949).
- ²² Platt, B. S., *Tables of Representative Values of Foods Commonly Used in Tropical Countries* (Med. Res. Council Spec. Rep. Ser. No. 302, HMSO, London, 1962).
- ²³ Kent-Jones, D. W., and Amos, A. J., *Modern Cereal Chemistry*, 9 (1967).
- ²⁴ Fraser, J. R., and Holmes, D. C., *J. Sci. Food Agric.*, 7, 589 (1956).
- ²⁵ *Nature*, 149, 460 (1942).
- ²⁶ *Nature*, 150, 538 (1942).
- ²⁷ *Nature*, 151, 629 (1943).
- ²⁸ *Nature*, 154, 582 (1944).
- ²⁹ *Nature*, 154, 788 (1944).

GENERAL

The Use of Correlational Analysis for Pattern Recognition

In contrast to spectral analysis¹, by which the presence of rhythmic activity can be detected but not defined in the time domain of a set of data, correlational analysis can be used to identify the exact time when a particular pattern, rhythmic or otherwise, occurs in the data². This can be done by defining a set of data as a template and "scanning" the noisy data with this template, computing the cross-correlation coefficient ($|r|$) at each data point. A high value of the correlation coefficient implies that the noisy data are similar to the template. When searching for complex wave shapes this method can have serious limitations because there may be small but complex parts of the template that are important in the definition or recognition of the pattern but which may contribute little to the cross-correlation coefficient.

Thus, the correlation coefficient may be sensitive to one part of the pattern; this effectively limits the extent to which the whole pattern can be recognized. For example, this can occur when the template includes high frequency components in one part of the template superimposed on or added to a low frequency component, which incorporates most of the area of the template. In that case the template will correlate highly and "recognize" slow waves not having the fast components of the template.

To avoid this we have developed a technique which allows us to divide the pattern to be recognized into two templates and to compute separate correlations for each; the two correlation coefficients are then multiplied together. The chief effect of this is to ensure that both parts of the pattern are recognized equally. The Recognition Index (RI) is the product of the two correlation coefficients when they are both positive. All cases in which the coefficients are of opposite sign and those for which they are both negative are ignored. Consequently, the scale reflects the degree to which both parts of the pattern, that is, the two templates that define the pattern, are correlated with the data at the appropriate time. The RI is the product of two correlation coefficients each of which can only vary between 0.0 and 1.0; it is a second order exponentially accelerated function and is independent of the amplitude of the matched data points that enter into the correlation.

A program for a PDP 12 computer has been written with an automatic feature which designates the data that have been correlated with the template for each RI occurring above an arbitrarily set threshold. The plotter output is shown in Fig. 1; the second trace (C-C) is the simple cross-correlogram of the whole of template A against the data shown below. High positive values occur at several points. The third trace (RI) shows the recognition index when the same template is separated into two parts, B I and B II, comprising a high frequency complex

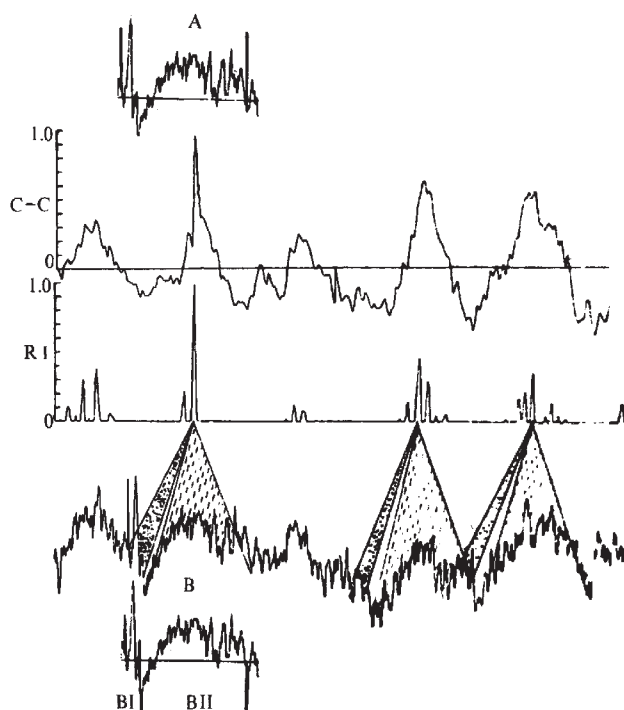


Fig. 1 Comparison of the cross-correlogram and the Recognition Index. Template A and template B encompass the same data; in template B the pattern to be recognized is separated into two features, B I and B II. Shaded areas encompass the parts of the data which enter into the correlations with template B. C-C, cross-correlation; RI, Recognition Index. Length of the base line of templates A and B = 2 s.

and a low frequency wave respectively, as shown below the data (template B). The data are the electrical activity of the brain recorded from the vertex and the pattern selected for recognition is one commonly known as the Contingent Negative Variation³; it includes a sharp evoked response (B I) and a slow wave (B II). The RI rises much more abruptly than the cross-correlogram because it is only when the evoked response and the slow wave are both coincident with the respective data that the correlations are high. This is clearly demonstrated by the patterns encompassed by radiating lines in the right half of the figure. The correlogram shows peaks at values of 0.65 and 0.60 whereas the RI shows peak values of 0.45 and 0.35, for the same patterns in the data. This occurs because the evoked potential encompassed by template B I is not present, although the slow waves are; consequently the RI is lower because its value, unlike the correlogram, is equally contingent on the presence of both features of the pattern. Further, measurement of the real time at which patterns similar to the template are present in the data is greatly enhanced by using the RI because of its greater discrimination³.

This work was supported by the National Research Council, Canada, and by the Clement and Jesse V. Stone Foundation.

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¹ Blackman, R. B., and Tukey, J. W., *Measurement of Power Spectra* (Dover, New York, 1958).

² Adey, W. R., Walter, D. O., and Hendrix, C. E., *Exp. Neurol.*, 3, 501 (1961).

³ Walter, W. G., Cooper, R., Aldridge, V. J., McCallum, W. C., and Winter, A. L., *Nature*, 203, 380 (1964).

BOOK REVIEWS

Responses to Skinner

Beyond Freedom and Dignity. By B. F. Skinner. Pp. 225. (Jonathan Cape: London, March 1972.) £2.25.

THE first task on receiving Skinner's book is to try and distinguish between what the book says and what the small army of reviewers and commentators have already said about it. As early as last December, it was evident from talking to Skinner that the reception of the book in the States had surprised even this most controversial of psychologists. Now, having read it, I share his surprise. It neither aims at, nor achieves, the impact of Skinner's earlier novel *Walden Two*, and it says nothing which is not implied in the underlying philosophy of the novel. Its style is neutral, if not colourless, whilst its statements are too repetitious for dramatic effect.

What is Skinner's message? His statement is familiar enough to those who have followed his career over the last forty years. He is tilting at the concept of "autonomous man", the mystical postulate to which man, by long tradition, has attributed his thoughts and actions. To Skinner autonomous is equivalent to miraculous. The struggle for freedom and dignity has been formulated as a defence of autonomous man whose actions are controlled by his "state of mind or internal feelings". The world of mind has stolen the show for Skinner. His science of behaviour will bring back the observable world and then ask how much is left to be explained. For Skinner, if for no one else, it is crystal clear; behaviour is controlled by its consequences and this implies that it is the environment which acts upon man, not man upon the environment. As a statement of a behaviourist's position this may be blunt but it is not novel, so why the controversy? Skinner, more than any other scientist, has the experimental evidence to show how far behaviour can be modified by rewarding animals for their responses. It would be foolish to argue against him on these grounds. But is he justified in claiming such generality for his findings? Does he not go beyond the evidence?

Skinner asserts that within our society control is often random in the sense that it has not always been deliberately planned and rewards and punishments may be arbitrary. He would abolish any form of punishment, to which he has always been opposed, but he would accept and plan systematically for positive forms of control. He does not consider it possible to free man from some kinds of control. Man is a biological organism reacting to the consequences of his responses: he should stop dissembling and come to terms with the forces that do in fact control his actions. For many this smacks of man as a puppet, being manipulated by society and whether it is by carrot or by stick makes little difference. Skinner may dislike the stick but the liberal thinker objects to both.

But is the case for control of man as simple as this? Skinner could cite many examples in the animal world where exact control is achieved, but will man's behaviour replicate such experiments? It is worth considering an example in a field where Skinner has made a notable contribution—the development of teaching machines. For Skinner our teaching system was ineffective because often it required no response from a student, and where it did, there was no immediate reinforcement of the response nor any provision for a student to set his own rate of responding. Skinner devised his linear programme and teaching machine to meet these conditions. No one would wish to deny the importance of this development and the success it has achieved in teaching difficult material. But, as usual, the answer turned out to be more complicated than it seemed at first. If we continue reinforcing every response with a correct answer this form of reinforcement ceases to be effective. Constant reinforcement does not continue to produce a constant result with human subjects, for students soon complain of boredom. The most beneficial effect of linear programmes has been in the careful analysis of material so that each step was logically developed from its predecessor. It became apparent to workers in this field that a number of pedagogical theories were much more

closely related than their authors had imagined and that concepts such as reinforcement, feedback, knowledge of results, confirmation and so on, were not the isolated entities they had been postulated to be. I would argue then that in the very field where Skinner's ideas have been applied successfully, the results have not worked out entirely as he would have predicted. They have been beneficial, but partly for other reasons. It is a familiar research and development story.

Where does this leave us? We may agree with Skinner on the role of the "environment in which the species evolved and in which the behaviour of the individual is shaped and maintained". There is, as one critic discovered, a striking similarity between Skinner's position and Robert Owen's, which Skinner himself points out. But Skinner, unlike his critic, also observes that most environmental experiments, such as Owen's at New Harmony, failed because the environments were constructed on the model of other environments in which the desired behaviour had been observed. In the new Utopias, alas, the behaviour failed to appear. For Skinner it is not enough to shift the emphasis from inner man to the environment; "we must know how the environment works before we can change it to change behaviour".

The significance of this to our present social-environmental problem is clear enough but many psychologists would feel that they too lack the evidence to say exactly how the environment influences behaviour. We have made a beginning and no one has contributed more than Skinner in predicting some of the consequences. In this book, because he has overstated his case for control and because his analysis of autonomous man is philosophically weak, it is a safe prediction that most attention will focus on these issues. This will only splash ink around. Skinner's basic tenet that behaviour is controlled by its consequences is fundamental to biological organisms and research needs to unravel some of its ramifications for mankind.

HARRY KAY

Volcanology

Volcanic Landforms and Surface Features. Edited by Jack Green and Nicholas M. Short. Pp. xxvi+519. (198 plates.) (Springer Verlag: Berlin and New York, 1971.) 116.50 DM; \$32.

THIS book has more than two hundred 29×19 cm pages of monochrome photographs of volcanoes, volcanic eruptions and structures of volcanic rocks, together with several of lunar features. The fourteen-page introduction by the late A. Poldervaart concisely reviews the whole field of volcanoes and their products, and defines most of the terms used. The book is rounded off by a glossary with between 500 and 1,000 entries and a useful collection of references. It aims to do for volcanology what *The Atlas and Glossary of Primary Sedimentary Structures*, by F. J. Pettijohn and P. E. Potter (Springer Verlag, 1964), did for sedimentology, but it does not succeed.

The photographs of volcanoes are, it is true, a pleasure to see (though they would have looked better on glossy paper) and convey an excellent impression of the great range shown in morphology and structure. Predictably, the very photogenic pahoehoe lava surfaces are well covered, but little is seen of the internal structure of lavas, and nothing is seen of the inside of an aa lava (except perhaps plate 76B in which some of the material described as "tuffaceous pyroclastics" may well be aa lava rubble seen in cross-section). The work is therefore of limited value to geologists working on pre-Quaternary volcanics who normally only see their rocks exposed in cross-section. It is the volcanoclastic rocks, however—the ones which most need treatment—which are dealt with least satisfactorily. The photographs are few and one cannot learn much from them or their captions. The only close-up of an outcrop of welded tuff (plate 168A) is a highly atypical example. A geologist who seeks guidance in distinguishing between the various kinds of volcanoclastic rock will be disappointed.

The captions to the photographs are of varied standard. Some carry much useful information and others very little. Some are unreliable: the cracks on breadcrust bombs are described (plate 161B) as shrinkage cracks"; it is stated (plate 162B) that "volcanic rocks carried in a nuée ardente do not show a serial change in vesicularity from rind to core", and the "pillow shaped structures in tuff" shown in plate 156B appear to be spheroidal weathering, while Anderson's observation of pahoehoe forming on the beach of Samoa is once again cited (plate 155C) as pillow lava.

In the introduction, "the presence of an unchilled, rolling upper surface pos-

itively identifies a flow" seems a dubious criterion by which to distinguish a lava flow from an intrusive sheet, and the common occurrence of offshoots from the latter intruded into its roof is not remembered. The old view is still maintained that the shape of bombs is due to "rotation in the air during flight" (also caption to plate 161C "aerodynamically shaped"). The captions to Figs. 3 and 4 are unfortunately transposed.

The glossary is in some ways less satisfactory than the introduction, for terms such as columnar jointing, composite lava, mantle bedding, spherulite, viscosity and xenolith are omitted and such strange entries as "burning mountain" and "ebullitim" (should this be ebullition?) included. I do not like the definition of gja: "a fissure from which volcanic eruptions take place. They may be filled with pyroclastics and lava as in the Norway-Greenland basin" (most Icelandic gjas have not erupted lava; the basin referred to is presumably Iceland). One could argue that a subaqueous tuff may be one accumulated under water and is not necessarily "formed by subaquatic eruptions", and it is quite wrong to say that acid lava, because it is stiff and viscous, "solidifies rapidly". Moreover the definitions given in the glossary and introduction do not always agree: for instance, coulee (I do not like the glossary definition: "an individual lava flow from the crater or flank of a cone forming a tongue-like extension down the cone").

This book is probably the largest and most comprehensive collection of volcanic photographs ever published, and it deserves a place on the shelf of every library of Earth sciences, although it is not cheap. However, it is unlikely to be as "acceptable to both students and professors in the universities" as the editors hoped, largely because they have not been sufficiently critical of its scientific content.

G. P. L. WALKER

A Quick Look at Optics

Introduction to Classical and Modern Optics. By Jurgen R. Meyer-Arendt. Pp. xi+558. (Prentice Hall: Englewood Cliffs, New Jersey, February 1972.) \$15.95.

FOR a fair assessment of this book it is necessary to remember that the author's aim has been to cover the whole field of optics at a reasonable level but also within a reasonable number of pages. The average length of the thirty-four sections is sixteen pages, with, for example, ten pages allocated to the section on apertures, pupils and fibre optics, fourteen to aberrations, twelve to interference, sixteen to the quantum nature of light, ten to electron optics,

eighteen to holography, and so on. This could well provide just what the non-specialist needs, although some readers may feel that they are being offered mere snippets of information. Nevertheless, thanks to the clarity and economy of the writing and the excellence of the diagrams, it should be possible to obtain a first understanding of the essential elements of most of the subjects discussed. In any case, each section includes some very useful suggestions for further reading, together with some problem questions. From time to time a relevant laboratory experiment is described, while the occasional biographical note of a Nobel prizewinner or some other optical giant of the past adds a human touch to the text.

The selection of material to be included (or excluded) is not always as happy as it might have been. Thus, the section on the velocity of light has a very old-fashioned look about it, while in the radiometry section Bunsen's grease-spot photometer is described as if it were a modern photometric technique instead of being 130 years old. And it would probably have been better to omit colorimetry altogether rather than squeeze two pages' worth into the quantum optics section!

W. D. WRIGHT

Early Essays

The Experimenters: a Study of the Accademia del Cimento. By W. E. Middleton. Pp. xv+415+6 plates. (Johns Hopkins: Baltimore and London, March 1972.) £10.70.

THE Accademia del Cimento of Florence has always fascinated scientists. It existed for very little more than ten years (1657–1667, approximately), and during that period rumours of its devotion to experiment combined with some news of the experiments it performed caused the learned world to await with great eagerness its research report, published in 1667 under the title *Saggi di Naturali Esperienze*, translated by Richard Waller in 1684 as *Essays of Natural Experiments*, "essay" being (correctly) used in its now obsolete sense of "first attempt" or "draft"—Dr Middleton translates the rather troublesome word "Saggi" as "examples". In the event, the scientific world was disappointed in the *Saggi*; the style (by Lorenzo Magalotti) was impeccable, but the experiments themselves had often been rendered out of date by the passage of time. Nevertheless the enterprise remains of interest, for the Accademia del Cimento was a fascinating blend of currents.

The patron and, as it were, President

of the Academy was Prince Leopold de' Medici, brother of Grand Duke Ferdinand of Tuscany. As Dr Middleton shows, Ferdinand was also actively interested in both scientific experiment and these particular experimenters. The experimenters themselves (not named in the *Saggi*) were eight. Of these only Borelli, Redi and Viviani are generally known today, although Carlo Rinaldini had a considerable reputation among his contemporaries. Redi seems not to have been very active and most of the effective experiments were devised by Borelli and Viviani, although Prince Leopold was energetic in designing experiments on freezing—a subject of perpetual fascination to Italians. One of Borelli's most interesting experiments—one that unfortunately did not appear in the *Saggi*—was a study of Saturn, in which a physical model was made of Saturn's ring as postulated by Huygens, which was viewed under various conditions by both trained and untrained observers to see whether the observed celestial phenomena could be repeated.

Dr Middleton has written an extremely thorough and scholarly study, based on the work of the eighteenth century scholar Giovanni Targioni Tozzetti and the original archives. He has described the sources, discussed the composition and functioning of the Academy and the biographies of its members, translated anew and annotated the *Saggi*, described unpublished experiments, the dissolution of the Academy, and its relations abroad. There is a great deal of information here.

MARIE BOAS HALL

Reactions with Proteins

Chemical Modification of Proteins. By Gary E. Means and Robert E. Feeney. Pp. x+254. (Holden Day: San Francisco and London, October 1971.) \$13.50 cloth; \$7.50 paperback.

It is most unfortunate for authors writing on protein chemistry and its applications that their work will inevitably be compared with Hirs's excellent and comprehensive treatise, *Methods in Enzymology*, volume 11. I can give no stronger recommendation than that this much smaller book stands up well to the comparison.

The division into two main sections is effective and the cross-referencing between them good. In the first part—a general discussion on why chemical modifications are important—it is very comforting to see Hammett plots presented and the relationship of reactivity to pK_a and environment stressed. This exposes the “black magic” approach that is often adopted in this field and the dangerous phrase “specifically re-

active” is refreshingly absent. This part ends with a chapter on the potential problems encountered. It will be very useful to research workers new to the field and students alike. The second part contains a detailed description of both the common and the unusual reagents used. Potential side reactions and the properties of the derivatives are discussed, together with techniques for estimating the extent of reaction. It is both comprehensive and readable—a combination not always found.

A small appendix describing a few experiments abstracted directly from the literature seems a little out of place. Research workers will surely read the original papers themselves, while others, student or non-specialist, do not require this degree of practical detail. The bibliography is extensive and there are many excellent tables that are individually referenced, which is a great convenience. Table 1-1 will be a boon to students. Unfortunately it contains an error, corrected in the text, stating that the reaction of maleic anhydride with sulphhydryl groups is reversible. This does not significantly detract from my feeling that this is a first-class book and that the paperback version at £2.95 makes Hirs's pandect at £15.40 seem rather an expensive luxury.

C. J. BRUTON

Planetary Exploration

Geological Problems in Lunar and Planetary Research. Edited by Jack Green. Pp. xiv+736. (AAS Publications: Tarzana California, 1971.)

THIS is an unusual book. It is a collection of papers, which in itself does not make it unusual these days except that it includes papers from not one but three symposia in the field of “extra-terrestrial geology” (an etymologically incorrect term but I think it is clear what I mean). But then not all the papers from the three symposia are there; the editor has done a pruning job to his satisfaction and included only a select few and then, for good measure, added a few others which had not been presented at any of the symposia but are relevant because they deal with the returned samples from the Apollo 11 and 12 missions, while the symposia took place (two in 1968 and one in 1969) before man's landing on the Moon. All this makes the volume dated in a sense; but much of the material deals not with an attempt at a grand reconstruction of lunar (or other planetary) history but with defining potential research problems related mainly to the Moon, but also to other planets as well, and with discussing the various exploration techniques. The symposia took place when the severe cuts in the Apollo

budget had not become a reality and one could look beyond Apollo 17 (now scheduled for December 10, 1972) to other future missions, up to a projected Apollo 20. Thus, although those papers which discuss bigger and better lunar rovers, or very deep drilling projects on the Moon seem, with hindsight, to be mere wishful thinking on the part of the aerospace engineers, there are other papers which present clearly the physical principles and limitations of remote sensing techniques or photogeology, the value of which has not been affected by the vagaries of Washington, DC.

The second unusual character of this volume is the style of some of the papers. They seem to be verbatim records of the symposia (including both papers and discussions thereof) and I get the impression that they must have been rather lively in character. One example is the paper by N. M. Short defending the impact theory of lunar morphology and its discussion (or dissection?) by editor Jack Green, a proponent of the volcanic theory. Unlike the recent Houston conference proceedings dealing with returned lunar samples, the present collection of papers is aimed at the broad scientific and engineering community. In fact, it resembles a sort of hand-out material which would excellently suit science reporters for national newspapers. There are five sections in the book: sensing techniques, phenomenology, exploration concepts, exploration methods and technology and, finally, “general subjects”. Under this last heading one finds a mixed bag that violently refuses to be classified under any of the previous headings but contains three interesting papers, one on water management on Earth, one attacking the plethora of mellifluous but etymologically incorrect terms (e.g., geocosmology, lunar geology, astrogeology and, of course, extra-terrestrial geology) and a final one on lunar “colonization”!

So, if you want to disregard the writing on the NASA wall and would like to have a middle-brow description of planetary exploration problems, go ahead and get a copy of this book. And why not? The best thing about this book is that it is free.

SUBIR BANERJEE

Adapting to Altitude

High Altitude Physiology: Cardiac and Respiratory Aspects. A Ciba Foundation Symposium. Edited by Ruth Porter and Julie Knight. Pp. xi+196. (Churchill Livingstone: Edinburgh and London, 1971.) £3.

NEARLY fifty years ago Haldane, Douglas and Fitzgerald performed their classic studies of the changes seen when

sea-level man ascends to altitude. Today, studies on the native born and resident at altitude predominate. These studies, pioneered by Professor Alberto Hurtado, in whose honour this symposium was held, have shown, for example, that the healthy native at high altitude hyperventilates, the lowered P_{CO_2} being compensated by a reduced plasma bicarbonate so that pH remains normal; and that he has a reduced alveolar-arterial P_{O_2} gradient, mild pulmonary hypertension and increased erythropoiesis leading to polycythaemia. Other, qualitative, differences include displacement of the haemoglobin dissociation curve due to increased 2,3-diphosphoglycerate in the erythrocytes. Hurtado has also stressed the changes at cellular level, including increased activity of enzyme systems linked to high-energy phosphate bond production.

Much of the work reported at this symposium springs from these observations. Studies on animals raised at altitude reveal an increase in lung volume relative to body weight, and hyperplasia of the carotid body. The latter is surprising because in man the increased ventilation probably results from enhanced responsiveness to CO_2 , the hypoxia response being "blunted". But further animal investigations are described which suggest a central origin of the blunted hypoxia response, peripheral chemoreceptor activity being undiminished.

Investigations into diseases resulting from the breakdown of altitude adaptation, such as chronic mountain sickness and high altitude pulmonary oedema, are included because they can aid our understanding of the mechanisms operative at altitude. The pattern of diseases other than those specific to altitude also varies. Thus ischaemic heart disease is relatively infrequent at altitude; this may be related to the greater vascularization of the heart and the altered enzyme concentrations in the myocardial cells reported here.

The origin of the greater adaptation of the native born at altitude remains obscure. Genetic factors seem unlikely since Sherpas and Andean natives show similar changes. But it seems to be necessary to be born at altitude for the full spectrum of adaptation to occur. This leads to the intriguing suggestion that intra-uterine life represents a hypoxic situation for which the foetus is well adapted, only to lose this adaptation when born at sea-level into an environment with increased oxygen availability.

The Ciba Foundation has again performed a valuable role in bringing together the clinician and the basic scientist, and this volume contains much to interest both the physiologist and the physician concerned with cardio-respiratory problems. N. JOELS

Mechanics Treatise

Lectures on Mechanics. (For Students of Physics and Engineering.) By J. Aharoni. Pp. viii+360. (Clarendon: Oxford; Oxford University: London, March 1972.) £8 boards; £4 paper.

THIS is not another textbook on mechanics in the usual English or American manner. In its additional coverage of elasticity and relativity, and its omission of practice exercises, it somewhat resembles continental *traités de mécanique*. It differs from these, on the other hand, by an idiosyncratic selection and organization of material, and by a discursive style backed by an abundance of excellent diagrams. Presumably these features were responsible for the title *Lectures* (albeit with a fine irony); at any rate the author states that the book stems from UNESCO courses to physicists and engineers. And in fact this bifid origin is plain to see in the resulting thick sandwich: a layer of Einstein-Minkowski space and Lorentz transformation, then a slab of elementary strength of materials and Newtonian (but not celestial) dynamics, lastly a layer of contact transformations and Hamilton-Jacobi theory.

Nothing worthwhile diffuses across the interfaces, however, and no preface explains the author's intentions. What, for example, can students of engineering gain from a first analysis of coupled pendulums *via* Hamilton's equations (chapter 18)? How will their appreciation of methodology be deepened by a bite at relativity, when nothing to the point is said about the concepts of mass and force in the context of engineering experimentation? As for students of physics, they will find here no trace of the spirit of modern continuum mechanics, in regard, for example, to the stress field-concept or Euler's moment of momentum postulate. Sadly, the scene is dominated by systems of "particles" (under binary reactions, of course) which shade imperceptibly into "bodies" by dint of terminology. In this vein, for example, a particulate version of Lagrange's virtual work principle (misattributed as usual to D'Alembert) is made to appear as the basis of all dynamics.

Yet parts of the book are good in isolation. I particularly liked chapter 17 for its attractive description of gyroscopic phenomena, and chapters 19-22 for their fresh and leisurely exposition of vibrations and Fourier analysis. And I imagine that chapter 10 on fixed-axis rotation, chapter 11 on statics of frames, and chapter 14 on elementary dynamics will be much to the taste of engineers. By comparison chapters 12 and 13 on elastostatics are pedestrian, unduly complicated, and marred by repeated errors of sign in figures and equations. And how came the author to permit himself

the topsy-turvy pronouncement that "isotropic bodies are the only ones of interest to civil and mechanical engineers"?! R. HILL

Quantum Electronics

Introduction to Quantum Electronics. By Paul Hlawiczka. Pp. xiv+443. (Academic: London and New York, December 1971.) £6; \$16.50.

THE author believes that a new engineering discipline is emerging, founded on quantum physics, and suggests the name "quantum electronics", based on parentage and dynamism. It includes not only masers and lasers, for which the term is already in use, but also semiconductor devices, electrical properties of gases, magnetic phenomena and superconductivity. Obviously one can think of other fields, for example many properties of metals, which could have been considered under the title.

The book is divided into three parts. The first deals in an elementary way with those subjects, mainly semiconductors, for which a complete quantum-mechanical treatment is not necessary. The second part deals with quantum mechanics, concentrating on those aspects which are necessary for the proper understanding of the third part, consisting of magnetic phenomena, superconductivity and lasers and masers. There are so many good books on quantum mechanics that much of the second part appears superfluous. A book at this level cannot be self-contained: one might as well have included a section on classical mechanics. This section on quantum mechanics is also axiomatic and not very useful as a first introduction.

The rest of the book on the contrary is very useful indeed and clearly reflects a profound teaching experience. Appropriate choice of material, a good balance between qualitative and quantitative treatment, and extreme lucidity will appeal to students of electronics and of physics, and to workers in related branches who look for an up-to-date reference work. Gratitude to the author would have been even greater if he had not here and there cut short his treatment by saying that further developments, or further explanations, are beyond the scope of the book. A notable definition glossed over is that of coherent radiation, which is only said to form part of a "well defined wave". There are several printing errors; for instance, in the table of constants a π is missing in the expression for ϵ_0 , and Rydberg has an additional h .

All in all, the volume is an excellent introduction to many applications of quantum physics. L. PINCHERLE

Obituary

Professor F. J. W. Roughton

THE recent death of Professor Francis John Worsley Roughton, FRS, brought to an end a scientific career which was unusual in its length of active and useful scientific work. It was more unusual in the breadth of interests represented, and quite exceptional in the number of separate, but related, new fields of scientific interest it opened up. Any one of these might have filled the working span of a lesser man, and each now has its own group of workers developing basic observations or ideas first put forward by Roughton. Curiously, there is no significant group of this kind in England, and this may have contributed to the relatively slight recognition his work received at home, compared with that given it abroad, especially in the United States.

Much of Roughton's work was concerned with time-dependent phenomena, and his first research project, with Professor H. Hartridge, was to measure the velocity with which oxygen combines with haemoglobin. To do this they developed the continuous flow rapid reaction method in which two liquids, in this case deoxyhaemoglobin and a solution of oxygen, were rapidly mixed together, and the streaming liquid viewed at varying distances along an observation tube, the distance serving as a measure of the time elapsed since mixing of the liquids. This work was done before photoelectric cells were generally available, and the ingenious method bore no relation to later procedures. It was quite otherwise with the principle, which has been developed by a series of workers, including G. A. Millikan and B. Chance, and culminated in the stopped-flow apparatus which has become an everyday laboratory instrument used in many chemical and biological disciplines. Interestingly, the time resolution achieved with the original apparatus was of the same order as that of its later descendants. There is a natural limit to what can be done with reasonable laboratory liquid driving pressures, and this limit was attained in a single stride.

Since Roughton's original intent had been to succeed his father (and four previous Roughtons) as a medical practitioner at Kettering, it was natural that he should turn to the physiological problem of gas exchange in heterogeneous systems once he had learnt that the oxygen reaction was rapid com-

pared with the time the erythrocyte spends in the capillaries. The combination of chemical reaction and diffusion in the erythrocyte continued to interest him for the remainder of his life, though he and his mathematical colleagues were handicapped by the lack of effective computing facilities. A further extension of interest to the reactions of carbon dioxide soon followed, and, having first shown that a catalyst of the CO_2 , water, carbonic acid reaction must be present in blood, he proceeded, with Meldrum, to work on carbonic anhydrase, and to develop the theory of carbon dioxide transport in blood. This work was summarized in an article in *Physiological Reviews* in 1935 which is still full of interest today. At about the same time he obtained evidence of the formation of carbamino haemoglobin by direct reaction of CO_2 with amino groups in the protein. The significance and validity of these observations were questioned for some time, but in the past 10 years, with Professor L. Rossi-Bernardi of Milan, the original observations were fully substantiated, and, making use of the new structural knowledge of the haemoglobin molecule, the dissociation constants of the active groups in the α and β chains were determined, and the interaction of CO_2 with 2,3-diphosphoglycerate defined. This was the work in which he was engaged at the time of his death and the most recent results have not yet been published.

The flow of his career was interrupted by a period of war-related research at Harvard, and, following his return to England and appointment to the chair of colloid science at Cambridge, he took up again the problem of determining the oxygen dissociation curve with sufficient accuracy to permit the evaluation of the four Adair constants which must describe the equilibrium of a tetrameric molecule. This involved the development of specially precise gasometric methods applicable to the extremes of the curve, up to 2 per cent saturation, and above 98 per cent saturation. The results showed that the equilibrium cannot be fully described by a simple two state model, such as that considered by Forbes and Roughton in 1931, in which a single conformation change occurs after three ligand molecules have been bound. He was, in general, sceptical about models, feeling that history had not been kind to those who forced the behaviour of haemoglobin into a predetermined

mould. During this later period he continued his contacts with his colleagues in the United States, and was concerned especially with projects of a physiological character. In all this work he had many colleagues and collaborators, and with continued bench work, his activities made for a full schedule which he continued, and delighted in, up to the very end of his life.

Professor B. G. Anan'ev

PROFESSOR BORIS GERASIMOVICH ANAN'EV, Dean of the Faculty of Psychology of Leningrad University, and one of the leading psychologists of the Soviet Union, died on May 18, 1972, after a short illness.

Anan'ev was born on August 14, 1907, in Vladikavkaz (now Ordzhonikidze). He graduated from the Gor'kii Pedagogic Institute in Vladikavkaz in 1928, and proceeded from there to a research course at the Bekhterev Brain Institute in Leningrad. After completing his postgraduate studies in 1930, he remained at the Bekhterev Institute until 1942. During the Second World War he was head of the psychological laboratory of a military casualty hospital. For the rest of his life his work was closely connected with Leningrad University, where he became a head of department and then Dean of the Faculty of Psychology. In 1951 he became head of the Institute of Pedagogic Research of the Academy of Pedagogic Sciences of the RSFSR (now the Academy of Pedagogic Sciences of the USSR). He was a member of the Praesidium of the Society of Psychologists of the USSR, a member of the Bureau of the Department of Psychology and Growth Physiology of the Academy of Pedagogic Sciences of the USSR, and a member of the Editorial Board of *Voprosy Psikhologii*.

Professor Anan'ev's principal fields of research were the study of sensations, transitions from sensory perceptions to thought, pedagogic psychology, psychopathology, growth psychology, and the history of psychology in Russia. His works include: *K. teorii vnutrennei rechi v psikhologii* (Towards a theory of inner speech in psychology) (1946); *Materialy k psikhologicheskoi teorii oshchushcheniya* (Materials for a psychological theory of sensation) (1948); *Assotsiatsiya oshchuschenii* (Association of sensations) (1955); and,

as co-author, *Osyazanie v protsessakh posnaniya i truda* (The sense of touch in processes of perception and work) (1959); *Novoe v uchenii o vozpriyatii prostranstva* (New work in the study of spatial perception) (1960); and *Problemy pedagogicheskoi antropologii* (Problems of pedagogic anthropology) (1966).

Announcements

International Meetings

September 5–7, **Recent Mathematical Developments in Control**, University of Bath (Secretary, Institute of Mathematics and its Applications, Maitland House, Warrior Square, Southend-on-Sea, Essex SS1 2JY).

September 6–8, **International Conference on Pressure Surges**, University of Kent, Canterbury.

September 11–14, **Calculation of Reaction Paths and Reaction Mechanisms**, Paris (Professor Simonetta, Institute of Physical Chemistry, University of Milan, Via Saldini 50, 20133 Milan, Italy).

September 12–14, **Decision, Design and the Computer**, London (I.Chem.E., 16 Belgrave Square, London SW1X 8PT).

September 12–20, **Second International Congress on the History of Oceanography**, Edinburgh (The Royal Society of Edinburgh, 22 George Street, Edinburgh EH2 2PQ).

September 14–19, **Isolation, Constitution and Biological Significance of Active Substances with Low Molecular Weight from Insects**, Varenna (Professor Dr M. Viscontini, Organischchemisches Institut der Universität, CH-8001, Zurich, Rami-strasse 76).

September 15–17, **Is Construction Destruction?** Norwich (Michael Oliver, Administrative Secretary of the JLO, Institution of Heating and Ventilation Engineers, 49 Cadogan Square SW1).

September 18–22, **Thermal Characterization of Polymers**, Bradford (B. M. Tidswell, University of Bradford, Yorkshire BD7 1DP).

Reports and Publications

not included in the *Monthly Books Supplement*
Great Britain and Ireland

Plant Breeding Institute, Cambridge. *Annual Report* for 1971. Pp. 160. (Cambridge: Plant Breeding Institute, 1972.) [86]
Overseas Development Institute. *Annual Report* for 1971. Pp. 42. (London: Overseas Development Institute, 1972.) [96]
Highlands and Islands Development Board. *Sixth Report* 1971. Pp. 96. (Inverness: Highlands and Islands Development Board, 1972.) 50p. [96]
Science Museum Library. *Science Library Bibliographical Series*, No. 798: Some References on the Effective Stimulus and the Transduction Mechanism of Olfaction and Gustation in Higher Vertebrates, 1950 to 1970. Pp. 4. (London: Science Museum Library, 1972.) [96]
Philosophical Transactions of the Royal Society of London. A: Mathematical and Physical Sciences. Vol. 272, No. 1222: Coordinate Perturbation and Multiple Scale in Gasdynamics. By L. Crocco. Pp.

275–301. 75p; \$2.10. Vol. 272, No. 1223: On Resistive Instabilities. By P. Baldwin and P. H. Roberts. Pp. 303–330. 75p; \$2.10. Vol. 272, No. 1224: Two-Dimensional Problems of Electrohydrostatic Stability. By D. H. Michael and M. E. O'Neill. Pp. 331–369. 75p; \$2.10. Vol. 272, No. 1225: Circular Islands as Resonators of Long-Wave Energy. By W. Summerfield. Pp. 361–402. £1.10; \$3.10. (London: The Royal Society, 1972.) [96]
Trent River Authority. *Annual Report* year ended 31st March, 1971. Pp. ii+118. (Nottingham: Trent River Authority, 1972.) [126]
The Molecular Basis of Antibiotic Action. By Professor Ernest F. Gale. (The St. John's College Cambridge Lecture 1971–72 delivered at the University of Hull, 3rd November 1971.) Pp. 20. (Hull: The Publications Committee, The University, 1972.) 30p net. [126]
University of Bristol: Department of Agriculture and Horticulture. Long Ashton Research Station (The National Fruit and Coder Institute)—*Report* for 1971. Pp. xxv+262. (Bristol: Research Station, Long Ashton, 1972.) £1.75. [126]
The Nutrition of Protected Crops. (Papers presented at the 2nd Colloquium of the Potassium Institute, Ltd., Kinsealy, Dublin, 1971.) (Colloquium Proceedings, No. 2.) Pp. 128. (Henley-on-Thames: The Potassium Institute, Ltd., 1972.) 85p. [126]
Science Research Council. *Greenwich Time Report* (Royal Greenwich Observatory). Time and Latitude Service, 1971 July–September. Pp. 225–240. (London: Science Research Council, 1972.) [126]
Biology and the History of the Future. An IUBS/Unesco Symposium with John Cage, C. G. Hedden, Margaret Mead, John Papaionnou, John Platt, Ruth Sager and Gunther Stent. Presented by C. H. Waddington, FRSc. Pp. vii+72. (Edinburgh: Edinburgh University Press, 1972.) 50p. [136]
J. J. Thomson Physical Laboratory, University of Reading. *Research Report* 1972. Pp. iii+57. (Reading: The University, 1972.) [136]
Airway, Vol. 1, No. 1, June 1972. (Monthly Journal of Britain's Civil Aviation Authority.) Pp. 8. (London: Civil Aviation Authority, 1972.) [136]
The Rational Use of Living Systems in Biomedical Research. Pp. 64. (Potters Bar, Herts.: The Universities Federation for Animal Welfare, 1972.) 40p. [146]
Advisory Committee on Oil Pollution of the Sea, Research Unit in the Rehabilitation of Oiled Seabirds. Recommended Treatment of Oiled Seabirds. Pp. 10. 25p. Second Annual Report of the Advisory Committee on Oil Pollution of the Sea. Pp. 32. 50p. (Newcastle upon Tyne: Research Unit on the Rehabilitation of Oiled Seabirds, Department of Zoology, The University, 1972.) [146]
Metric Units, Conversion Factors and Nomenclature in Nutritional and Food Sciences—Report of the Subcommittee on Metrication of the British National Committee for Nutritional Sciences. Pp. 16. (London: The Royal Society, 1972.) [146]
Department of the Environment. *Forest Products Research 1971: Report of the Director of Forest Products Research*. Pp. 18. (Aylesbury: Forest Products Research Laboratory, 1972.) [146]
The British Industrial Biological Research Association. *Annual Report* for 1971. Pp. 58. (Woodmansterne Road, Carshalton, Surrey: BIBRA, 1972.) [156]
Northern Ireland. Ministry of Commerce—Geological Survey of Northern Ireland. *Regional Geology of Northern Ireland*. By H. E. Wilson. Pp. x+105+18 plates. (Belfast and London: HMSO, 1972.) 50p net. [156]
International Diagnostic Aids Limited—*Product Guide*. (Portslade, Brighton: International Diagnostic Aids Limited, 1972.) [156]
Migraine. Pp. 28. (London: Office of Health Economics, 1972.) 25p. [156]
University of Cambridge. *Report of the Head of the Department of Engineering* for the year 1970/1971. Pp. 22. (Cambridge, The University, 1972.) [156]
University of Oxford. *Institute of Economics and Statistics—Annual Reports, 1964–1970*. (Supplement No. 7 to the *University Gazette*, May 1972.) Pp. 31. (Oxford: The University, 1972.) 50p. [166]
Council for National Academic Awards. *Annual Report* for 1970/71. Pp. 64. (London: Council for National Academic Awards, 1972.) [166]
Standard Methods for the Analysis of Tobacco Smoke. Compiled and edited by K. Rothwell and C. A. Grant. (Research Paper No. 11.) (London: Tobacco Research Council, 1972.) [166]
Titles of Dissertations approved for the Ph.D., M.Sc., and M.Litt. Degrees in the University of Cambridge during the Academic Year 1970–1971. Pp. 40. (Cambridge: Board of Graduate Studies, The University, 1972.) [196]
Bulletin of the British Museum (Natural History). Zoology. Vol. 22, No. 8: Recent Records of Mammals (other than Bats) from Ethiopia. By G. H. Corbet and D. W. Yalden. Pp. 211–252. (London: British Museum (Natural History), 1972.) £1.55. [196]
Courtaulds Report and Accounts, 1971–1972. Pp. 24. (London: Courtaulds Limited, 1972.) [206]
German Documentary Theatre. By Professor A. V. Subiotto. (Inaugural Lecture delivered in the University of Birmingham on 17 February 1972.) Pp. 16. (Birmingham: The University, 1972.) 25p. [216]
Department of Trade and Industry. *Technology and the Environment*, No. 3, May 1972—Reports from Scientific Counsellors (Vehicles, Transportation, Traffic). Pp. 40. (London: Department of Trade and Industry, 1972.) [216]
Friends of the Earth. *Whale Campaign Manual*. Pp. 93. (London: Friends of the Earth, 1972.) [216]
Irwin. *Science Teaching Equipment: Physics—*

Electronics—Mechanics—Secondary Science—Nuffield. Pp. 166. (Croydon: Irwin and Partners, Ltd., 1972.) [216]

The University of Leeds. *Publications and Titles of Theses, 1968–69*. Pp. 134. *Publications and Titles of Theses, 1969–70*. Pp. 149. (Leeds: The University, 1972.) [226]

The Scientific Proceedings of the Royal Dublin Society. Series A. Vol. 4, No. 9: The Pre-Caledonian Rocks of the Mullet Peninsula, County Mayo, Ireland. By J. S. Sutton. Pp. 121–136+plates 8 and 9. 60p. Vol. 4, No. 10: Cleavage Polymorphism in Conifers and Taxads—a Survey. II. Cupressaceae, Pinaceae and Conclusions. By J. Doyle and M. Brennan, SJ. Pp. 137–158. £1. Vol. 4, No. 11: Award of the Boyle Medal to Patrick J. Nolan, Ph.D., D.Sc. Pp. 159–160. 10p. Vol. 4, No. 12: The Photoelectric Nucleus Counter. By Patrick J. Nolan. (Boyle Medal Lecture.) Pp. 161–180. 75p. Vol. 4, No. 13: The Pleistocene History of the Irish Sea—Second Approximation. By G. F. Mitchell. Pp. 181–200. 75p. Vol. 4, No. 14: The Silurian and Devonian Inlier of Knockshigowna Hill, County Tipperary, Ireland. By B. M. Pendergast. Pp. 201–212. 50p. Vol. 4, No. 15: Hybridization Nuclei on *Brassica* Plants. By P. L. Curran. Pp. 213–218+plate 9. 30p. (Dublin: Royal Dublin Society, 1972.) [236]

The Dialectical Myth. By Joseph Stucky. Pp. 24. (Hoddesdon, Herts: The St. Gregory Publishing Company, 1970.) 35p. [236]

University of Oxford. *Annual Report of the Curators of the Bodleian Library for 1970/1971*. Pp. 52. (Oxford: The University, 1972.) 75p. [236]
Cement and Concrete Association. *Report for the year 1971*. Pp. 54. (London: Cement and Concrete Association, 1972.) [236]

The Gladiolus Annual 1972—being the Yearbook of The British Gladiolus Society. Edited by L. Plumridge. Pp. 98. (Shoreham by Sea: P. Hollowat, Hon. Secretary, British Gladiolus Society, 1972.) [266]

Building Research Station Digest, No. 142: Fill and Hardcore. Pp. 4. (London: HMSO, 1972.) 5p. [266]

National Extension College, Cambridge. *Geography, GCE 'A' Level—Lessons 1–10*. (Cambridge: National Extension College, 1972.) [266]

Tweed River Purification Board. *Eighteenth Annual Report* for the year ended 31st December, 1971. Pp. 35. (Newtown St. Boswells: Tweed River Purification Board, 1972.) [266]

The *Zoological Record*. 1967, Vol. 104, Section 20: List of New Genera and Subgenera recorded in Volume 104. Compiled by H. O. Ricketts. Pp. 18. 1969, Vol. 106, Section 18: Aves. Compiled by the Staff of The Zoological Society of London. Pp. 297. £9; \$21.70. (London: The Zoological Society of London, 1972.) [266]

The Family Planning Association. *40th Report and Accounts, 1971–72*. Pp. 48. (London: Family Planning Association, 1972.) [266]

U.K. Petroleum Industry Statistics—Consumption and Refinery Production, 1970 and 1971. Pp. 8. (London: Institute of Petroleum, 1972. Published on behalf of the UK Petroleum Industry Advisory Committee.) [276]

The Zoological Society of London. *Scientific Report, 1969–1971*. Pp. 499–610. (*J. Zool. Lond.*, 1972, 166.) (London: Zoological Society of London, 1972.) [276]

University of Oxford. *Eighth Annual Report of the Delegates of the Science Area* for the year ending 31 July 1971. Pp. 143. (Oxford: The University, 1972.) 75p. [286]

Department of the Environment. *Welsh Office. Statistics for Town and Country Planning. Series II: Floorspace. No. 2: Floorspace in Industrial, Warehouse, etc., Shopping and Office Use—Total Stock as at 1 April 1967 and changes April 1967 to March 1968. England and Wales*. Pp. xxix+110. (London: HMSO, 1972.) £1.45 net. [286]

TRADA 71: Report of the Director of the Timber Research and Development Association for the year 1971. Pp. 16. (London: Timber Research and Development Association, 1972.) [286]

The Lister Institute of Preventive Medicine. *Report of the Governing Body 1972*. Pp. 41. (London: The Lister Institute of Preventive Medicine, 1972.) [296]

Cancer Research Campaign. *49th Annual Report 1971, incorporating Research Supported during 1972*. Pp. 143. (London: Cancer Research Campaign, 1972.) [296]

The Royal Observatory, Edinburgh. *Report of the Astronomer Royal for Scotland for the Year Ending 31st March 1972*. Pp. 13. The Royal Observatory, Edinburgh, 1822–1972. (Survey of the Observatory's history and review of its present activities.) Pp. 36. (Edinburgh: The Royal Observatory, 1972.) [296]

Cotton Research Corporation. *Annual Report* for 1971. Pp. 18. (London: Cotton Research Corporation, 1972.) [306]

University of Lancaster. *Higher Education Bulletin*, New Series, Vol. 1, No. 1, May 1972. Pp. 56. (Lancaster: The University, 1972.) 35p. [306]

International Tin Research Council. *Annual Report of the Tin Research Institute for 1971*. Pp. 40. (Greenford, Middlesex: Tin Research Institute, 1972.) [306]

Other Countries

Australia: Commonwealth Scientific and Industrial Research Organization. *Annual Report of the Division of Chemical Physics, 1970/1971*. Pp. 44. (Clayton, Victoria: CSIRO, 1972.) [105]

- Publications of the United States Naval Observatory, Second Series. Vol. XX, Part 4: Optical Study of Nearby Galaxies. By Harold D. Ables. Pp. 126. Vol. XXII, Part 2: Micrometer Measures of 1,343 Double Stars. By Charles E. Worley. Pp. 136. (Washington, DC: Government Printing Office, 1971.) [105]
- Republique Française. Office de la Recherche Scientifique et Technique Outre-Mer. Mémoires ORSTOM, No. 54: Les Sols à Profil Calcaire Différencié des Plaines de la Basse Moulouya (Maroc Oriental). Par A. Ruellan. Pp. 302. Travaux et Documents de l'ORSTOM. Les Elements Traces dans les Sols. Par H. Aubert et M. Pinta. Pp. vi + 97. Etude Experimentale de l'Action des Animaux sur l'Humification des Matériaux Vegetaux. 1. Premieres Experiences et Conclusions Preliminaires. Par G. Bachelier. Pp. 75. Plantes Médicinales du Congo-Brazzaville-Uvriopsis, Pauridiantha, Diospyros. Para Armand Bouquet. Pp. 112. (Paris et Bondy: ORSTOM, 1971 et 1972.) [125]
- Comptes Rendus des Travaux du Laboratoire Carlsberg. Vol. 38, Nos. 19-20: The Effects of Salts on the Enzymatic Activity of Subtilisin Type Carlsberg and Subtilisin Type Novo. By M. Ottesen and I. Svendsen. The Inhibitory Effects of Alcohols and Guanidine Hydrochloride on the Enzymatic Activity of the Subtilisins. By I. Svendsen. Pp. 369-398. 11.50 D.kr. Vol. 38, No. 21: Selective Ion Absorption in Various Plant Species and Its Ecological Significance. By C. Olsen. Pp. 399-422. 11.50 D.kr. Vol. 38, No. 22: Plasma Membrane Permeability and Pinocytosis in *Chaos chaos*. By Philip W. Brandt and K. B. Hendil. Pp. 423-444. 11.50 D.kr. Vol. 38, No. 23: Use of Reductive Methylation for Radioactive Labelling of Proteins. By M. Ottesen and B. Svensson. Pp. 445-456. 11.50 D.kr. (Copenhagen: Danish Science Press, Ltd., 1971 and 1972.) [155]
- Forschungsbericht (IV) der Bundesregierung. Pp. 216. (Bonn: Der Bundesminister für Bildung und Wissenschaft, 1972.) [155]
- World Meteorological Organization. Technical Note No. 120: Review of Forecast Verification Techniques. By Professor E. M. Dobryshman. Pp. 51. Technical Note No. 121: Dispersion and Forecasting of Air Pollution. Report by a working group of the Commission for Atmospheric Sciences, prepared by R. E. Munn, A. E. J. Eggleton, L. Facy, D. H. Pack and F. H. Schmidt. Pp. 116. (Geneva: World Meteorological Organization, 1972.) [155]
- United States Department of the Interior: Geological Survey. Water-Supply Paper 1986: Sediment Transport and Tidalinity in the Eel River Basin, California. By William M. Brown, III, and John R. Ritter. Pp. vi+70. 50 cents. Water-Supply Paper 1999-1: Water for Cranberry Culture in the Cranmore Area of Central Wisconsin. By Louis J. Hamilton. Pp. iii+20+2 plates. Professional Paper 521-E: Stratigraphy of the Cretaceous Rocks and the Tertiary Ojo Alamo Sandstone, Navajo and Hopi Indian Reservations, Arizona, New Mexico, and Utah. By R. B. O'Sullivan, C. A. Repenning, E. C. Beaumont and H. G. Page. Pp. iv+65+ plates 1 and 2. Professional Paper 663-A: Pre-Quaternary Rocks in the Sun River Canyon Area, Northwestern Montana. By Melville R. Mudge. Pp. vi+142+3 plates. (Washington, DC: Government Printing Office, 1971 and 1972.) [155]
- Nuclear Public Relations Contact Group. The Nuclear Controversy. (A collection of papers prepared by members of the NPRCG for the Eleventh General Meeting of the Group.) Pp. 79. (Rome: Nuclear Public Relations Contact Group, c/o Forum Italiano dell'Energie Nucleare, Via Paisiello, 26/28, 1972.) [165]
- Expédition Antarctique Belgo-Néerlandaise 1966. Sondages Ionosphériques Riometrie, Base Roi Baudouin, Février 1966 à Février 1967. Par C. Stelling. Pp. 348. (Bruxelles: Exantar, 1 Rue de Louvain, 1970.) [165]
- Australia: Commonwealth Scientific and Industrial Research Organization. Annual Report of the Division of Animal Physiology, 1970. Pp. 106. (Sydney: CSIRO, 1972.) [175]
- Records of the Australian Museum, Sydney. Vol. 28, No. 8: *Bassianobdella fissa* SP. Nov. (Hirudinoidea: Richardsoniidae), with an Initial Demonstration of Systematic Values in the Lengths of Annulli in the Mid-Nephric Somites. By Laurence R. Richardson. Pp. 129-139. 70c. Vol. 28, No. 9: Australasian *Pectinisetia* Stein, with Notes on the Genus (Diptera: Muscidae). By Adrian C. Pont. Pp. 141-160. \$1. (Sydney: The Australian Museum, 1972.) [175]
- Australian Journal of Zoology, Supplementary Series, No. 11: A Revision of *Strongylurus* Hope (Coleoptera: Cerambycidae: Cerambycinae) including a Description of the Male Genitalia. By H. J. Elliot and F. J. D. McDonald. Pp. 20. No. 12: Australian and the New Guinea "Picture-Wing" Species of the Genus *Monoleha* Kieffer (Diptera: Ceratopogonidae). By Margaret L. Debenham. Pp. 40. (East Melbourne, Victoria: Editorial and Publications Section, CSIRO, 372 Albert Street, 1972.) [175]
- Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Bulletin 212: Lower Cambrian Trilobites from the Sekwi Formation Type Section, Mackenzie Mountains, Northwestern Canada. By W. H. Fritz. Pp. 58+20 plates. (Ottawa: Information Canada, 1972.) \$4. [175]
- State of California. The Resources Agency: Department of Fish and Game. Fish Bulletin No. 154: Californian Marine Fish Landings for 1970. By Robert R. Bell. Pp. 50. (Long Beach, California: Marine Technical Information Center, California State Fisheries Laboratory, 1971.) [175]
- Annals of the Transvaal Museum. Vol. 27, No. 11: Observations on the Percy Fyde Nature Reserve Tsessebe Population. By B. J. Huntley. Pp. 225-240 (plates 20 and 21). Vol. 27, No. 12: Notes on Psammophilous Scorpions and a Description of a New Species (Arachnida: Scorpionidae). By Gerald Newlands. Pp. 241-254 (plate 22). Vol. 27, No. 13: A Study of the Biology of Monteiro's Hornbill. By A. C. and M. I. Kemp. Pp. 255-268 (plate 23). Vol. 27, No. 14: Reports from the Mammal Research Unit: 5. Fossil *Suncus* (Mammalia: Soricidae) from Southern Africa. By J. Meester and I. J. Meyer. Pp. 269-278. (Pretoria: Transvaal Museum, 1972.) [175]
- National Council on Radiation Protection and Measurements, Washington. NCRP Report No. 40: Protection Against Radiation from Brachytherapy Sources—Recommendations of the National Council on Radiation Protection and Measurements. Pp. vi+65. (Washington, DC: NCRP Publications, P.O. Box 30175, 1972.) \$2. [185]
- Journal of Supramolecular Structure, Vol. 1, No. 1, 1972. Edited by C. Fred Fox. Pp. 1-76. Subscription price: Volume 1, 1972, 6 issues \$35; outside US add \$3 for postage. (New York: Alan R. Liss, Inc., 1972.) [185]
- National Center for Atmospheric Research, Boulder, Colorado. Particulate Models: Their Validity and Application. (A Workshop held at the National Center for Atmospheric Research, Boulder, Colorado, 21 August 1970.) Edited by I. H. Blifford, Jr. Pp. viii+284. (Boulder, Colorado: NCAR, 1972.) [185]
- Föredrag vid Pyroteknikdagen 1971, Stockholm den 10 Maj 1971. Pp. 105. (Jönköping, Sweden: The Secretary, Teknisk Stig Johansson, Sektionen för Detonik och Förbränning, Box 608, 1972.) 50 Sw. cr. [225]
- Office de la Recherche Scientifique et Technique Outre-Mer, ORSTOM. Mémoire Ostron No. 52: Tradition et Changements dans la Société Guéer. Par Alfred Schwartz. Pp. 259. (Paris et Bondy: Office de la Recherche Scientifique et Technique Outre-Mer, 1971.) 90 francs. [225]
- US Department of the Interior: Geological Survey. Water-Supply Paper 1970-A: Floods of May 1968 in South Arkansas. By R. C. Gilstrap. Pp. vi+94+plate 1. (Washington, DC: Government Printing Office, 1972.) \$1. [235]
- Smithsonian Studies in History and Technology, No. 13: The Consul General's Shanghai Postal Agency, 1867-1907. By Peter L. Kofsky. Pp. v + 46. 60 cents. Smithsonian Contributions to the Earth Sciences, No. 8: Late Quaternary Progradation and Sand Spillover on the Outer Continental Margin Off Nova Scotia, Southeast Canada. By Daniel J. Stanley, Donald J. P. Swift, Norman Ailverberg, Noel P. James, and Robert G. Sutton. Pp. iv+88. \$1.25. Smithsonian Contributions to Paleobiology, No. 13: Upper Miocene Echinoids from the Yorktown Formation of Virginia and their Environmental Significance. By Porter M. Kier. Pp. 41 (10 plates). 55 cents. Smithsonian Contributions to Zoology, No. 116: New Species and Further Notes on the Tetranychidae Mostly from the Southwestern United States (Acarina: Tetranychidae and Tenuipalpidae). By Edward W. Baker and Donald M. Tuttle. Pp. iii+37. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) [235]
- Companhia de Diamantes de Angola (DIAMANG). Servicos Culturais. Dundo—Lunda—Angola. Museu do Dundo. Publicacoes Culturais. No. 83: Subsídios para a Historia. Arqueologia e Etnografia dos Povos da Lunda. Contos dos Quicocos: Recolhidos e Traduzidos por Joao Vicente Martins (Museu do Dundo). Vorwort, Einleitung, Kommentar, Literatur-, Namen- und Sachverzeichnis. Von Harald de Sicard. Pp. 260. (Lisboa: Companhia de Diamantes de Angola, 1971.) [235]
- Office de la Recherche Scientifique et Technique Outre-Mer, ORSTOM. Mémoires ORSTOM No. 55: Les Philébotomes de la Région Ethiopienne (Diptera, Psychodidae). Par E. Abonnenc. Pp. 285. (Paris et Bondy: Office de la Recherche Scientifique et Technique Outre-Mer, 1972.) [235]
- Republic of South Africa: Department of Industries. Division of Sea Fisheries Investigation Report, No. 89: The Cape Fur-Seal *Arctocephalus pusillus*. 4. Estimates of Population Size. By R. W. Rand. Pp. 28. (Sea Point, Cape Town: Director of Sea Fisheries, 1972.) [245]
- Three Thousand Million Years of Plant Life in Africa. By Edna P. Plumstead. (Alex. L. du Toit Memorial Lectures, No. 11.) Pp. 72+25 plates. (Johannesburg: The Geological Society of South Africa, 1972.) [245]
- Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Paper 71-41: Geomathematical Evaluation of Copper and Zinc Potential of the Abitibi Area, Ontario and Quebec. By F. P. Agterberg, C. F. Chung, A. G. Fabbri, A. M. Kelly and J. S. Springer. Pp. vii+55. (Ottawa: Information Canada, 1972.) \$2. [245]
- Australia: Commonwealth Scientific and Industrial Research Organization. Annual Report of the Division of Textile Physics, 1970/1971. Pp. 21. (Sydney, CSIRO, 1972.) [265]
- Centre National pour l'Exploitation des Océans, Bureau de Recherches Géologiques et Minières. Mémoires du BRGM No. 79: Colloque sur la Géologie de la Manche, organisé par l'Association des Géologues du Bassin de Paris les 14 et 15 Janvier 1971 à Paris. Pp. 326. (Paris: Editions du BRGM, 1972.) [265]
- Australia: Commonwealth Scientific and Industrial Research Organization. CSIRO Directory 1972. Pp. 31. (Canberra: CSIRO, 1972.) [265]
- The Population Council Annual Report 1970. Pp. 175. (New York, NY: The Population Council, 245 Park Avenue, 1972.) [305]
- Stora Kopparbergs Bergslags AB—Annual Report for 1971. Pp. 28. (Falun, Sweden: Stora Kopparbergs Bergslags AB, 1972.) [305]
- US Department of the Interior: Geological Survey. Water-Supply Paper 2014: Quality of Surface Waters of the United States, 1967. Parts 7 and 8: Lower Mississippi River Basin and Western Gulf of Mexico Basins. Pp. xv+814. (Washington, DC: Government Printing Office, 1972.) \$3.50. [305]
- Annals of the South African Museum. Vol. 58, Part 1: The Material Culture of the Cape Nguni. Part 1: Settlement. By E. M. Shaw and N. J. Van Warmelo. Pp. 1-101+17 plates. Vol. 59, Part 7: A New Species of *Paradoxostoma* (Crustacea, Ostracoda) from South Africa. By K. G. McKenzie. Pp. 133-137. Vol. 59, Part 8: Development of *Trachurus trachurus* (Carangidae), The South African Maasbanker. By E. H. Haigh. Pp. 139-150. (Cape Town: South African Museum, 1972.) [16]
- Smithsonian Contributions to Botany, No. 6: Flora Morphology and Systematics of *Lamouroxia* (Scrophulariaceae: Rhinanthoideae). By Wallace R. Ernst. Pp. 63. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) \$1.25. [16]
- Instituto Antártico Argentino, Buenos Aires. Contribuciones. No. 133: Estudio de la Eliminación de 17-Cetosteroides y 17-Hidroxicorticosteroides Urinarios a Traves de 4 Años en Hombres que Vivieron en la Estación Científica "Almirante Brown" (Antártida). Por J. E. Varela de Rodríguez et al. Pp. 34. No. 135: Algunos Aspectos de la Cartografía Antártica—La Napoteca del Instituto Antártico Argentino. Por S. B. Kaplun de Schauer. Pp. 10. No. 143: Pulsaciones Aurales en Frecuencias Medias. Por H. A. Cazenueve. Pp. 30. No. 140: Las Floras Fósiles de Antártida Occidental y sus Relaciones Estratigráficas. Por H. A. Orlando. Pp. 12. (Buenos Aires: Dirección Nacional del Antártico, Instituto Antártico Argentino, 1971.) [16]
- Shrimps and Prawns of Southern Africa. By Brian Kensley. Pp. 65. (Cape Town: South African Museum, 1972.) [16]
- Geological Survey of Western Australia. 1:250,000 Geological Series—Explanatory Notes. Cambridge Gulf, Western Australia, Sheet SD/52-14 International Index. Compiled by K. A. Plumb and J. J. Vevers. Pp. 30. Drysdale and Londonderry, W.A., Sheets SD/52-5 and 9 International Index. Compiled by D. C. Gellatly and J. Sofoulis. Pp. 19. Prince Regent and Camden Sound, Western Australia, Sheet SD/51-15, International Index. Compiled by I. R. Williams and J. Sofoulis. Pp. 16. Bulletin 122: Geology of the Western Australian part of the Eucla Basin. By D. C. Lowry. Pp. 201. (Perth: Geological Survey of Western Australia, 1969, 1970 and 1971.) [16]
- Australian Journal of Botany, Supplementary Series, No. 3: A Review of the Family Pittosporaceae in Papuasia. By R. Schodde. Pp. 60. (East Melbourne: Editorial and Publications Section, CSIRO, 1972.) [26]
- US Department of Health, Education and Welfare—Food and Drug Administration. Low and Very Low Dose Influences of Ionizing Radiations on Cells and Organisms, Including Man: a Bibliography. By Benjamin P. Sonnenblick. Pp. vii+325. (Rockville, Md.: US Department of Health, Education and Welfare, Food and Drug Administration, 1972.) [26]
- International Journal of Polymeric Materials, Vol. 1, No. 1, September 1971. Edited by Herman S. Kaufman. Pp. 1-110. Subscription rates (per volume of 4 issues, post paid): Libraries, \$47; £19.60. Individuals who warrant that the journal is for their own use and order direct from the publisher \$17; £7.10. (New York, London and Paris: Gordon and Breach Science Publishers, 1972.) [26]
- Publications of the National Research Council of Canada, Supplement 1970. Pp. iv+153. (Ottawa: National Research Council of Canada, 1972.) [26]
- Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Paper 71-32: Geochemical and Biogeochemical Exploration Methods Research in the Cobalt Area, Ontario. By E. H. W. Hornbrook. Pp. iv+45. \$2. Paper 71-33: Regional Geochemical Exploration in the Coppermine River Area, District of Mackenzie, a Feasibility Study in Permafrost Terrain. By R. J. Allan, J. J. Lynch and N. G. Lund. Pp. vii+52. \$2. Paper 71-35: Three Geochemical Standards of Sulphide-Bearing Ultramafic Rock: U.M.1, U.M.2, U.M.4. Compiled by E. M. Cameron. Pp. 10. 75 cents. Paper 72-9: Recommended Standards for Recording the Location of Mineral Deposits. By A. M. Kelly. Pp. vii+8. 75 cents. (Ottawa: Information Canada, 1972.) [56]
- Higher Education, Vol. 1, No. 2, May 1972. (An International Journal of Higher Education and Educational Planning.) Pp. 141-266. (Amsterdam: Elsevier Publishing Company, 1972.) [56]
- Smithsonian Contributions to Zoology, No. 113: A Monographic Study of the Subfamily Tiphinae (Hymenoptera: Tiphidae) of South America. By Harry W. Allen. Pp. iii+76. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) \$1.25. [56]
- National Multiple Sclerosis Society. Annual Report for 1971. Pp. 40. (New York: National Multiple Sclerosis Society, 1972.) [56]
- Republique Française. Office de la Recherche Scientifique et Technique Outre-Mer. Travaux et

Documents de l'ORSTOM No. 15: Maintenance Sociale et Changement Economique au Sénégal. I. Doctrine Economique et Pratique du Travail chez les Mourides. Par J. Copans, Ph. Couty, J. Roch et G. Rocheteau. Pp. 274 (Paris et Bondy: Office de la Recherche Scientifique et Technique Outre-Mer, 1972.) 36 francs. [166]

Science Council of Canada. Issues in Canadian Science Policy. (A Commentary on some aspects of Vol. 2 of the Report of the Senate Committee on Science Policy.) Pp. 13. (Ottawa: Science Council of Canada, 1972.) [166]

Exploring Yellowstone. By Ruth Kirk. Pp. 120. (Seattle and London: University of Washington Press, 1972. Published in co-operation with Yellowstone Library and Museum Association.) \$2.95 paper; \$5.95 cloth. [76]

Australia. Annual Reports of the Defence Standards Laboratories. Department of Supply, 1970-1971. Pp. 66. (Maribyrnong, Victoria: Defence Standards Laboratories, 1971.) [76]

Rhodesia. Report of the Trustees and Director of the National Museums of Rhodesia for the year ended 31st December, 1971. Pp. 32. (Bulawayo, Salisbury and Umtali: National Museums of Rhodesia, 1972.) [86]

International Atomic Energy Agency. Technical Reports Series, No. 60: Laboratory Training Manual on the Use of Radionuclides and Radiation in Animal Research. Third edition. (A Joint Undertaking by the Food and Agriculture Organization of the United Nations and the IAEA.) Pp. 174. (Vienna: IAEA; London: HMSO, 1972.) 120 Austrian schillings; £2; \$5. [86]

National Geographic Society. Washington. Research Reports: Abstracts and Reviews of Research and Exploration authorized under grants from the National Geographic Society during the years 1955-1960. Edited by Paul H. Oehser. Pp. x+205. (Washington, DC: National Geographic Society, 1972.) [86]

Meteorologisk Institut gennem Hundrede År, 1872-1972. Pp. 328. (Copenhagen: Udgivet af det Danske Meteorologisk Institut, 1972.) [86]

Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Paper 69-36: Surficial Geology of Northern Yukon Territory and Northwestern District of Mackenzie, Northeast Territories. By O. L. Hughes. Pp. v+11. \$1.50. Paper 71-27: Rocks and Minerals for the Collector—La Ronge-Creighton, Saskatchewan; Flin Flon-Thompson, Manitoba. By Ann P. Sabina. Pp. vii+100. \$2. (Ottawa: Information Canada, 1972.) [96]

Zoological Museum, University of Copenhagen. Steenstrupia, Vol. 2, No. 10: Atollidae in the Zoological Museum of Copenhagen (Coelenterata, Scyphomedusae). By P. L. Kramp and Peter Blanner. Pp. 157-165. (København: Zoologisk Museum, 1972.) [96]

United States Department of the Interior: Geological Survey. Professional Paper 708: Ground-Water Hydraulics. By S. W. Lohman. Pp. vii+70+9 plates. Water-Supply Paper 1880-C: Summary of Floods in the United States during 1967. By J. O. Rostvedt et al. Pp. vi+115. 75 cents. (Washington, DC: Government Printing Office, 1972.) [96]

Council of Europe. Nature Conservation Handbook for Local Authorities. By J. B. de Villemorin. (Nature and Environment Series.) Pp. 72. (Strasbourg: Council of Europe, 1971.) gratis. [126]

Mycoplasmataceae: a Bibliography and Index, 1852-1970. By C. H. Domermuth and J. G. Rittenhouse. (Research Division Bulletin 61.) Pp. 136. (Blacksburg, Virginia: Virginia Polytechnic Institute and State University, 1972.) [126]

The Life History of Douglas Fir. By George S. Allen and John N. Owens. Pp. x+139. (Ottawa: Information Canada, 1972.) gratis. [126]

The Surveillance and Prediction of Volcanic Activity: a Review of Methods and Techniques.

(Earth Sciences, 8.) Pp. 166. (Paris: Unesco; London: HMSO, 1971.) 56 francs; £4.20; \$14. [126]

Sur la Périodicité et les Perturbations Astronomiques du Mécanisme Terrestre. Par Georges Dubourdieu. Pp. 67. On the Periodicity and Astronomic Disturbances of the Earth's Mechanism. By Georges Dubourdieu. Pp. 47. (Meudon, France: Collège de France, Laboratoire de Géologie, 1972.) [126]

The Carlsberg Foundation's Oceanographical Expedition Round the World 1928-30 and previous "Dana" Expeditions. "Dana" Report No. 81: Bramidae. By Giles W. Mead. Pp. 166+9 plates. (Copenhagen. Andr. Fred. Host and Son, 1972.) 75 D.kr. [126]

Annual Report of the Council for Tobacco Research—USA, Inc., for the year ending June 30, 1971. Pp. 95. (New York: The Council for Tobacco Research—USA, Inc., 1972.) [136]

The Medications Physicians Prescribe: Who Shall Determine the Source? Pp. 28. (Washington, DC: Pharmaceutical Manufacturers Association, 1972.) gratis. [146]

Smithsonian Contributions to Zoology, No. 116: New Species and Further Notes on the Tetranychidae Mostly from the Southwestern United States (Acarina: Tetranychidae and Tenuipalpidae). By Edward W. Baker and Donald M. Tuttle. Pp. iii+37. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) 45 cents. [146]

Académie Royale de Belgique. Annuaire 1972, CXXXVIII. Pp. 328+143. (Bruxelles: Académie Royale de Belgique, 1972.) [156]

World Health Organization. International Agency for Research on Cancer, Lyon, France—Annual Report for 1971. Pp. 128. (Geneva: WHO; London: HMSO, 1972.) 3 Sw. francs; 30p; \$0.75; Fr.f. 4. [156]

Alfred P. Sloan Foundation. Report for 1971. Pp. viii+72. (New York: Alfred P. Sloan Foundation, 1972.) [156]

US Department of the Interior: Geological Survey. Professional Paper 456-C: The Hallett Volcanic Province, Antarctica. By Warren Hamilton. Pp. iv+62. (Washington, DC: Government Printing Office, 1972.) 70 cents. [156]

Smithsonian Studies in History and Technology No. 16: Living Historical Farms Handbook. By John T. Schlebecker and Gale E. E. Peterson. Pp. iii+91. 65 cents. Smithsonian Contributions to Botany. No. 7: *Thespesia populnea* (L.) Solander ex Correa and *Thespesia populneoides* (Roxburgh) Kostelecky (Malvaceae). By F. R. Fosberg and W. H. Sacht. Pp. 13. 25 cents. No. 8: Three Indo-Pacific Thelypteris Species Reinterpreted and a New African Species Described. By F. R. Fosberg and M. H. Sacht. Pp. 10. 25 cents. Smithsonian Contributions to Zoology. No. 101: An Ecological Reconnaissance of Wilpattu National Park, Ceylon. By John F. Eisenberg and Melvyn Lockhart. Pp. v+118. \$1.50. No. 103: Gammaridean Amphipoda of Australia, Part 1. By J. Laurens Barnard. Pp. vi+333. \$3.25. No. 113: A Monographic Study of the Subfamily Tiphinae (Hymenoptera: Tiphidae) of South America. By Harry W. Allen. Pp. iii+76. \$1.25. (Washington, DC: Smithsonian Institution Press, 1972. For sale by US Government Printing Office.) [156]

Bulletin of the American Museum of Natural History, Vol. 147, Article 5: The Systematics of the North American Family Baenidae (Reptilia, Cryptodira). By Eugene S. Gaffney. Pp. 241-320. (New York: American Museum of Natural History, 1972.) \$3.95. [156]

Bell Laboratories 1971. Pp. 20. (Murray Hill, NJ: Bell Laboratories, 1972.) [156]

Instituto Antartico Argentino, Buenos Aires. Direccion Nacional del Antartico. Divulgacion No. 2: Operacion 90. Pp. 64. Antartida, No. 1, Diciembre de 1971. Pp. 64. Contribucion No. 124: Contribucion Argentina a la Observacion de Auroras

en la Region Subauroral y Minauroral. Por Jorge G. Gomez. Pp. 24. (Buenos Aires: Instituto Antartico Argentino, 1971.) [156]

Proceedings of the Centennial Convocation of the Thayer School of Engineering at Dartmouth College, held September 23 to 25, 1971, in commemoration of the opening of the Thayer School, September 20, 1971. Edited by William P. Kimball and The Convocation Speakers. Pp. v+193. (Hanover, New Hampshire: The Thayer School, Dartmouth College, 1972.) \$5. [156]

The Michelson and Morley Experiment and Real Causes of its Failure. By Sharadchandra Tipnis. Pp. 12. (Kolhapur: S. Tipnis, 1963 'B' Ward, Mangalwar Peth, 1972.) [166]

In Partnership with Nature: Unesco and the Environment. By Daniel Behrman. Pp. 115. (Paris: Unesco, 1972.) [196]

Académie Royale de Belgique. Mémoires de la Classe des Sciences. 2e Série. T. XL, Fasc. 2: Structure de Roation des Bandes 0-0 à 13-0 du Système de Schumann-Runge de la Molécule d'Oxygène. Par F. Biauque. Pp. 66. T. XL, Fasc. 3: Topologies Localement Solides dans les Espaces Vectoriels Préordonnés. Par Michel Duhoux. Pp. 62. (Bruxelles: Académie Royale de Belgique, 1972.) [196]

Gesellschaft für Strahlen- und Umweltforschung mbH., München. Jahresbericht 1971 Kurzfassung. Pp. 204. (München: Gesellschaft für Strahlen- und Umweltforschung, mbH., 1972.) [196]

World Health Organization. Technical Report Series. No. 487: WHO Expert Committee on Specifications for Pharmaceutical Preparations—Twenty-fourth Report. Pp. 86. 6 Sw. francs; 60p; \$1.50. No. 490: Techniques for the Collection and Reporting of Data on Community Water Supply—Report of a WHO Scientific Group. Pp. 24. 3 Sw. francs; 30p; \$0.75. No. 491: The Planning and Organization of a Health Laboratory Service—Fifth Report of the WHO Expert Committee on Health Laboratory Services. Pp. 36. 5 Sw. francs; 40p; \$1. No. 493: WHO Expert Committee on Smallpox Eradication—Second Report. Pp. 64. 5 Sw. francs; 50p; \$1.25. No. 494: The Etiology and Prevention of Dental Caries—Report of a WHO Scientific Group. Pp. 19. 3 Sw. francs; 30p; \$0.75. No. 495: Opiates and their Alternatives for Pain and Cough Relief—Report of a WHO Scientific Group. Pp. 19. 3 Sw. francs; 30p; \$0.75. (Geneva: WHO; London: HMSO, 1972.) [196]

Republique Francaise. Office de la Recherche Scientifique et Technique Outre-Mer. Travaux et Documents de l'ORSTOM, No. 15: Maintenance Sociale et Changement Economique au Sénégal. I. Doctrine Economique et Pratique du Travail Chez les Mourides. Par J. Copans, Ph. Couty, J. Roch et G. Rocheteau. Pp. 274. (Paris et Bondy: Office de la Recherche Scientifique et Technique Outre-Mer, 1972.) 80 francs. [196]

List of Worthwhile Life and Health Insurance Books. 1972 edition. Pp. 78. (New York: Institute of Life Insurance, 277 Park Avenue, 1972.) [206]

Académie Royale de Belgique. Mémoires de la Classe des Sciences. 2e Série. T. XL, Fasc. 1: Revision Systématique des Daurades du Genre Dentex de la Côte Africaine Tropicale Occidentale et de la Méditerranée. Par Max Poll. Pp. 51. (Bruxelles: Académie Royale de Belgique, 1971.) [206]

Tätigkeitsbericht Deutsche Forschungsgemeinschaft 1971. Pp. 270. Programme und Projekte Deutsche Forschungsgemeinschaft 1971. Pp. 683. (Bonn-Bad Godesberg: Deutsche Forschungsgemeinschaft, 1972.) [206]

Republique de Côte d'Ivoire: Ministère de l'Economie et des Finances. Esquisse Structurale de la Côte d'Ivoire: Essai de Géotectonique Regionale. Par Bernard Tagini. Pp. 302. (Abidjan: Société pour le Développement Minier de la Côte d'Ivoire, 1971.) [206]

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